ABSTRACTS OF WORLD MEDICINE

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Pathology

1. On the Origin of the Pulmonary Hyaline Membranes
H. N. HADDERS and M. N. J. DIRKEN. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **70**, 419–425, 1955. 8 figs., 16 refs.

An experimental study on anaesthetized, full-grown rats is reported from the State University, Groningen, Netherlands, in which various fluids were given by direct injection from the back into the lungs. Injections of rabbit serum and of solutions of histamine and "euphyllin" (theophylline and ethylenediamine) all led to the formation of hyaline membrane, whereas injection of amniotic fluid failed to do so. This supports the view that in infants the formation of hyaline membrane is due to transudation of plasma and not to the inspiration of amniotic fluid.

A. C. Lendrum

CHEMICAL PATHOLOGY

2. Tubeless Gastric Analysis. An Evaluation of Azure A Indicator Compound
J. T. GALAMBOS and J. B. KIRSNER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 752–756, Dec., 1955. 1 fig., 6 refs.

The examination of the gastric contents by means of intubation and test meals has many disadvantages which have gradually led to its decreasing use, but the recent introduction of tubeless analysis with ion-exchange resins has greatly simplified the procedure. In the study here reported from the University of Chicago the authors employed azure A indicator compound, as originally described by Segal *et al.* (*Gastroenterology*, 1955, **28**, 402; *Abstracts of World Medicine*, 1955, **18**, 350) instead of quinine resin, which occasionally gives false results. Specimens of urine were collected exactly at the end of the first and second hours, and the amount of dye excreted was determined spectrophotometrically after conversion of the colourless form by a simple procedure into blue azure A compound.

Of the 104 patients investigated, 84 secreted hydrochloric acid after histamine stimulation and 20 were achlorhydric. Of these 20 patients, 16 excreted no azure A dye at all, the output of the remaining 4 ranging from 0·1 to 0·29 mg. in the 2-hour excretion period, while of the other 84 patients, 82 excreted more than 0·5 mg. and 71 patients more than 0·6 mg. azure A compound in the 2-hour period. No quantitative correlation was present between the urinary azure A content and the amount of hydrochloric acid in the gastric juice.

The authors conclude, nevertheless, that azure A compound administered orally after adequate histamine stimulation reliably differentiates patients with achlorhydria from those secreting hydrochloric acid.

Z. A. Leitner

3. A Quantitative Modification of the "Tubeless" Gastric Analysis
P. B. DONOVAN and W. J. TIGHE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 895–899, Dec., 1955. 3 figs., 13 refs.

The technique of tubeless gastric analysis depends on the power of the hydrogen ions of the free hydrochloric acid in the gastric juice to displace the quininium ion from a quinine-containing resin. Some of the displaced quinine is absorbed from the small intestine and excreted in the urine, where it may be detected and estimated by means of its fluorescence in ultraviolet light. Many reports comparing the results by this method with those of the conventional intubation procedure in large groups of both normal subjects and dyspeptic patients have been published, and it is generally agreed that the correlation between the two methods is uniformly good in cases of achlorhydria. However, no quantitative relationship has been shown to exist between the amount of quinine excreted in the urine and the acidity of the gastric juice, expressed as the concentration of free HCl.

The present authors consider that the urinary quinine excretion should be more closely related to the total number of available hydrogen ions present in the gastric juice, that is, to their concentration multiplied by the volume of the aspirated juice. At the Rees-Stealy Clinic, San Diego, California, they have therefore studied 101 patients by both methods; if no free acid was found to be present in the aspirated sample of fasting gastric juice, then 0·2 mg. of histamine was injected subcutaneously and the tests repeated. The total available hydrogen ion content of the juice was calculated from the volume and concentration of each aspirated specimen as the equivalent volume of N/10 HCl. When the mean values thus obtained were plotted against the mean values of urinary quinine excretion a straight-line relationship was obtained, the line being represented by the formula: $X=\frac{(Y-82)}{7\cdot3}$, where X is the gastric acidity in millilitres of N/10 HCl, and Y the urinary excretion of quinine in microgrammes.

In view of these results the authors suggest that the use of "tubeless" gastric analysis could be extended

beyond its application as a mere screening test for achlorhydria to replace the usual intubation method in many situations. *M. J. H. Smith*

4. Evaluation of Clinical Methods in Gastrointestinal Diseases. VII. Tubeless Detection of Gastric Acidity Using an Azure A Ion-exchange Indicator

A. A. GOLDBLOOM, M. A. FEINSTEIN, and H. B. EIBER. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **22**, 288–291, Oct., 1955. 23 refs.

The intubation method of obtaining specimens of gastric contents for analysis is time-consuming, unpleasant for the patient, and not always practicable. The tubeless method, which involves the use of an ion-exchange resin, has proved simple, and the results are comparable in accuracy with those of analysis of specimens obtained by intubation. At the New York Medical College–Metropolitan Medical Center gastric acidity was determined in 40 patients, both the above methods being used in each patient. In the tubeless method a control sample of urine was obtained one hour after administration of a capsule containing 250 mg. of caffeine sodium benzoate. The patient was then given 2 g. of azure A carboxylic resin indicator compound (" diagnex improved ") and the urine collected 2 hours afterwards. The control specimen was diluted with water to the same specific gravity as the 2-hour test specimen and the colours compared with standards. A greenish tinge in the 2-hour specimen of urine denoted in most instances the presence of free gastric hydrochloric acid, and the intensity or paleness of the greenish tinge was a measure of hyper- or hypo-acidity. The green tinge was absent from the control urine.

In the present investigation there was complete agreement between the results obtained by the two methods. *L. A. Elson*

5. Serum Glutamic Oxalacetic Transaminase as an Index of Hepatocellular Integrity

D. W. MOLANDER, F. WRÓBLEWSKI, and J. S. LADUE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 831–839, Dec., 1955. 5 figs., 5 refs.

Glutamic oxaloacetic transaminase (G.O.T.) is an enzyme concerned in the transfer of the α-amino group of aspartic acid to α-ketoglutaric acid, resulting in the formation of glutamic and oxaloacetic acids. It is widely distributed in the tissues, particularly in cardiac muscle and liver, and tissue damage such as that which follows acute myocardial infarction releases the enzyme into the blood, causing an increased activity in the serum. As described in a previous paper (*Ann. intern. Med.*, 1955, **43**, 345; *Abstracts of World Medicine*, 1956, **19**, 259) the authors observed a striking elevation of serum G.O.T. activity in 2 patients exposed to carbon tetrachloride. Both patients recovered and the enzymic activity in the serum fell rapidly to normal within one week.

In order to assess the possible usefulness of serum G.O.T. activity estimations in following the progress of liver regeneration after acute injury the authors, in a study carried out at Cornell University Memorial Center, New York, measured the serum G.O.T. activity in rats which had been given carbon tetrachloride by intubation. Blood was obtained by cardiac puncture and the enzymic activity estimated spectrophotometrically. The results showed that the degree and duration of the rise in serum G.O.T. activity was proportional to the amount of carbon tetrachloride administered and also to the severity of the centrilobular zonal necrosis of the liver as assessed histologically. They conclude that the level of serum G.O.T. activity appears to be a highly specific index of hepatocellular injury, that it is more sensitive than determination of the serum cholinesterase or alkaline phosphatase value, and may be a useful means of assessing the progress of restoration of normal liver architecture after acute injury. *M. J. H. Smith*

6. Optical Density of Serum in Cancer. Comparison with Findings in Patients Having Other Diseases and in Normal Persons

J. A. QUINN, S. A. KATZ, and A. E. RAPPOPORT. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 1128–1147, Oct., 1955. 3 figs., 3 refs.

The authors describe, from Youngstown Hospital, Youngstown, Ohio, a test for the presence of cancer which is based on measurement of the optical density of the serum. An [unusually thorough] attempt was made to assess the reliability of the test under varying conditions by determining the frequency of false positive and false negative results in patients with cancer, patients suffering from other diseases, and healthy persons, a total of 1,736 individuals being examined. A positive result was recorded in 282 (90·1%) of 313 patients with histologically proved cancer; a negative result was obtained in 817 (86·3%) of 944 non-cancerous patients, and in 466 (97·7%) of 479 presumably healthy persons. Among the patients with cancer early cases of the disease gave a higher rate of positive reactions than advanced cases [an interesting and possibly important fact]. The highest rate of false negative results was observed among the cases of cancer of a highly anaplastic type, or in which general dissemination had occurred. Most of the false positive results among the non-cancerous patients occurred in cases of acute inflammation and degenerative disease, or in pregnant women. *M. H. Salaman*

7. Determination of 5-Hydroxy-indole-acetic Acid in Urine and its Excretion in Patients with Malignant Carcinoids

A. HANSON and F. SERIN. *Lancet* [*Lancet*] **2**, 1359–1361, Dec. 31, 1955. 2 figs., 19 refs.

At the General Hospital, Malmö, Sweden, the authors studied the excretion of 5-hydroxy-indole-acetic acid in 8 patients with malignant abdominal carcinoid proved by microscopy. A qualitative screening test for the rapid examination of urine from suspected cases of carcinoid, and a simple quantitative method for estimating the urinary concentration of 5-hydroxy-indole-acetic acid in such cases are described. The methods are based on the reaction between 5-hydroxy-indole-acetic acid and Ehrlich's aldehyde reagent. While this reaction is not specific for 5-hydroxy-indole-acetic acid, it is considered

that the method is applicable to the investigation of patients with carcinoid because paper chromatography has shown that 5-hydroxy-indole-acetic acid is the predominant abnormal metabolite in the urine of such patients. *H. Harris*

HAEMATOLOGY

8. The Detection of a Latent Antibody in ABO Hemolytic Disease

C. McNeil, E. F. Trentelman, R. J. Wherritt, C. D. Fullner, and V. Kreutzer. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 888–894, Dec., 1955. 15 refs.

During a previous large-scale study of blood groups in habitual abortion (*Amer. J. clin. Path.*, 1954, **24**, 767; *Abstracts of World Medicine*, 1955, **17**, 4) the authors encountered a number of heterospecific matings in which the mother failed to reveal immune anti-A or anti-B antibody. In this further paper from the University of Utah College of Medicine they describe 2 cases in which immune anti-A antibody was first found 3 weeks post partum. Discussing the source and nature of the inhibiting substance that masked the antibodies before parturition they suggest the following hypotheses: (1) that the infant produced an A-like substance which was ineffectual after delivery; (2) that the mother produced a substance that counteracted her own anti-A antibody; or (3) that a neutralizing placental product was the antibody-suppressing substance.

Suggestions for further research are put forward. In the meantime the authors make the following recommendations: (1) that ABO grouping as well as Rh typing should be carried out on expectant mothers; (2) that Group-O mothers as well as Rh-negative mothers should be regarded as potential bearers of infants with haemolytic disease, and the husband's blood group should also be determined; (3) a direct cord-blood elution test for the presence of anti-A and anti-B antibody should be performed, particularly if the Coombs and Witebsky neutralization tests have given negative results. It seems to be proved that replacement transfusion with Group-O blood is effective in controlling ABO haemolytic disease of the newborn. *A. Piney*

9. The A and B Antigens on Human Platelets Demonstrated by Means of Mixed Erythrocyte–Platelet Agglutination. [In English]

R. R. A. Coombs and D. Bedford. *Vox sanguinis* [*Vox Sanguinis* (*Amst.*)] **5**, 111–115, Dec., 1955. 2 figs., 3 refs.

The presence of iso-antigens cannot be demonstrated with certainty on platelets by using platelet suspensions alone. However, by adopting the principle of mixed agglutination the authors, working at the University of Cambridge, were able to confirm the statements of other workers that A and B antigens are to be found on platelets. The method used is as follows. A platelet suspension is incubated at room temperature with anti-A or anti-B grouping serum. The platelets are then washed and added to a suspension of erythrocytes of the appropriate ABO group, and the results are read by phase contrast microscopy. A positive reaction is shown by the development of mixed erythrocyte and platelet agglutination.

It is suggested that " the principle of this method may be applied to investigations on the antigenic structure of other body cells ". *A. W. H. Foxell*

10. Clotting Factor X. Physiologic and Physicochemical Properties

F. Duckert, P. Flückiger, M. Matter, and F. Koller. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **90**, 17–22, Oct., 1955. 4 figs., 12 refs.

From the University of Zürich the authors describe the demonstration of a new clotting factor, Factor X, by matching experiments with serum from patients given " marcoumar " (3-(1-phenylpropyl)-4-hydroxycoumarin) or with hepatitis (both deficient in the new factor) and from patients with haemophilia B (deficient in Factor IX). Its isolation by adsorption on barium sulphate is described, the affinity of Factor X for barium sulphate being greater than that of Factors VII or IX.

Factor X is shown to be a thromboplastin accelerator which is distinct from Factors VII and IX. Its presence is postulated to explain the delay in thromboplastin generation which is observed with serum from a patient treated with marcoumar. The defect is not corrected by serum from a marcoumar-treated patient receiving vitamin K_1 and therefore replete in Factor VII, or by serum from a patient with haemophilia B, which supplies Factor IX. The addition of purified Factor X to the serum of a marcoumar-treated patient restores normal thromboplastin generation. The possibility that the results are due to a slight deficiency of Factor IX or to an excess of antihaemophilic globulin is discussed and discarded, as also is the possible influence of the thrombin in serum from haemophilia B. *Mary D. Smith*

11. The Coagulation Defect Caused by Tromexan Therapy

A. S. Douglas. *Clinical Science* [*Clin. Sci.*] **14**, 601–613, Nov., 1955. 10 figs., 31 refs.

In the study here reported from the Radcliffe Infirmary, Oxford, the author presents new evidence in support of the concept that anticoagulant drugs of the coumarin group, in particular ethyl biscoumacetate (" tromexan "), cause a deficiency not only of prothrombin, but also of Factor VII (cothromboplastin, proconvertin). He also describes experimental evidence indicating some interference with blood thromboplastin formation. Using two-stage methods of prothrombin assay, he showed that in the plasma of 14 patients given tromexan the deficiency of prothrombin was considerably less than that of Factor VII. Further, comparison with the results in a case of idiopathic prothrombin deficiency appeared to confirm that the prolonged one-stage clotting time in the blood of patients receiving tromexan therapy is largely a manifestation of deficiency of Factor VII rather than of prothrombin deficiency.

An assessment is also made of other methods used in determination of the prothrombin content of " coumarin plasma ". The method in which Russell's viper venom and lecithin are employed is shown to reflect the deficiency of prothrombin, but to be insensitive to the deficiency of Factor VII. Interference with the formation of blood thromboplastin was demonstrated when " tromexan serum " was substituted for normal serum in performing the thromboplastin generation technique. It was also shown that there was a prolongation of the whole-blood clotting time in silicone-treated tubes, and that prothrombin consumption was delayed in the blood of patients receiving tromexan. *A. Brown*

12. **The Prothrombin Consumption Time in the Presence of Haemolysate. Its Application to the Diagnosis and Treatment of Haemophilia.** (Le temps de consommation de la prothrombine en présence d'hémolysat. Son application au diagnostic et au traitement de l'hémophilie)
P. IZARN, C. V. HUSSÉY, and A. J. QUICK. *Sang* [*Sang*] 26, 633–649, 1955. 3 figs., 21 refs.

In this paper from Marquette University School of Medicine, Milwaukee, the authors describe the use of haemolysate as an aid to the diagnosis of haemophilia. Haemolysate is defined as the product of haemolysis by freezing of washed erythrocytes which have been suspended in physiological saline. It prolongs the prothrombin consumption time (P.C.T.) of normal blood and also of platelet-free plasma. It is not identical with the coagulation Factors V or VII, but appears to act as an activator of thromboplastinogen (antihaemophilic globulin) and is closely bound to haemoglobin. That the sensitivity of the P.C.T. test is increased by this substance was shown by the fact that in 70 normal subjects the P.C.T., which ranged from 17 to 41 seconds, was increased to 40 to 150 seconds on addition of haemolysate. There is no such increase in cases of severe haemophilia, but in milder and latent forms of the disease haemolysate produces a slight prolongation of the P.C.T.

The method of preparation of haemolysate is as follows: 9 ml. of blood is collected into a siliconed syringe containing 1 ml. of 0·1M solution of sodium oxalate, from which it is transferred into silicone-coated tubes and centrifuged at 1,000 r.p.m. in a horizontal position for 5 minutes. The supernatant plasma, which is rich in platelets, is drawn off and replaced by an equal volume of physiological saline; the contents of the tube are mixed and again centrifuged, this procedure being repeated three times, at 2,000 r.p.m. for 20 minutes. After the final centrifugation the deposit is resuspended in a volume of physiological saline equal to that of the original volume of plasma. The suspension is then frozen for at least 12 hours at a temperature of −20° C., at which it can be kept for 60 days. Total haemolysis occurs when the specimen is allowed to return to room temperature.

For the performance of the P.C.T. test 0·1 ml. of the serum under examination is added to a mixture containing 0·1 ml. each of deprothrombinated rabbit plasma (as a source of Factor V), 0·02M solution of calcium chloride, and rabbit brain extract. The time to the formation of a clot is measured from the moment of addition of the serum. The test is then repeated in the presence of haemolysate, 0·1 ml. of haemolysate being added before coagulation to each 2 ml. of the blood or 1 ml. of plasma under test. The tube is then inverted twice to ensure mixing and placed in a water bath at 37° C.; 15 minutes after coagulation it is centrifuged and returned to the bath for a further 45 minutes. The prothrombin time of the serum is then determined as above. " Native " plasma is obtained by centrifuging the patient's fresh, non-oxalated blood in a silicone tube at 800 r.p.m. for 5 minutes at a temperature of +4° C.

It is claimed that this test enables the observer to determine the quantity of thromboplastinogen in the blood of haemophiliacs during treatment. When the P.C.T. in the presence of haemolysate is less than 30 seconds haemorrhage is inevitable unless plasma is given immediately. When a P.C.T. of 50 to 70 seconds is recorded plasma need not be given for 24 hours.
A. W. H. Foxell

13. **Demonstration of the L.E. Factor by the Anti-globulin Consumption Reaction.** (Mise en évidence du facteur L.E. par la réaction de consommation d'anti-globuline)
P. MIESCHER. *Vox sanguinis* [*Vox Sanguinis* (*Amst.*)] 5, 116–120, Dec., 1955. 7 refs.

The author describes a technique by which he claims to demonstrate that the L.E. factor is a gamma globulin having the characteristics of a leucocytic antinuclear antibody.

[The evidence does not appear to be conclusive that such an antibody acts specifically on the leucocyte nucleus.] *A. W. H. Foxell*

14. **A Study of the Morphology of the Living Cells of Blood and Bone Marrow in Supravital Films with the Phase Contrast Microscope. II. Blood and Bone Marrow from Various Hematologic Dyscrasias**
G. A. ACKERMAN and N. C. BELLIOS. *Blood* [*Blood*] 10, 1183–1203, Dec., 1955. 60 figs., 25 refs.

From Ohio State University College of Medicine, Columbus, the authors describe in considerable detail the appearance of the cells of the blood and bone marrow in various blood diseases compared with normal cells of the same lineage studied in supravitally stained films by phase contrast and bright field microscopy. They conclude that in leukaemia there is morphological evidence of impaired cellular metabolism, the changes being quantitative rather than qualitative. Subsequently they state that certain changes may occur " which have been considered to represent ' sarcomatous alterations ' " and which are due to irreversible changes in the metabolic pattern of the cell rather than the reversible arrest of maturation of the leukaemic cell. The appearance of the cells in certain anaemias and in thrombocytopenia is briefly described.

[The paper is illustrated by ten full-size plates each containing reproductions of 6 photomicrographs of blood

cells in various pathological conditions as seen by phase contrast microscopy when stained by supravital methods, yet no pictures of normal cells are included for direct comparison.] *Janet Vaughan*

MORBID ANATOMY AND CYTOLOGY

15. **The Nature of Endocardial Fibrosis in Childhood.** (Zur Kenntnis der Endokardfibrose im Säuglingsalter)
E. STRESEMANN. *Archiv für Kreislaufforschung* [*Arch. KreislForsch.*] **23**, 77–95, Dec., 1955. 5 figs., bibliography.

The author describes in detail the gross anatomical and the histological findings in 4 infants with endocardial fibroelastosis examined post mortem at the Lübeck Pathological Institute. Although in one of the cases fibroelastosis was associated with a bicuspid pulmonary valve and in another with a patent ductus arteriosus at the age of 5 months, all 4 were of the " idiopathic " type and none of the type which is found in cases of congenital hypoplasia of the mitral valve and left ventricle, frequently associated with aortic stenosis or obliteration. Of particular interest is the description of lesions, not previously reported, in the conductive system. There was fibrosis of the sino-auricular node, in which elastic fibres were present in one case, and in other cases there was oedema of the Aschoff–Tawara node with occasional cellular infiltration.

The changes in the subendocardial muscle fibres in this condition are considered by the author to be secondary and due to metabolic factors. The presence of a definite layer of plain muscle fibres in a thickened endocardium at an age of less than 2 years is regarded as characteristic of fibroelastosis. The various theories concerning the pathogenesis of this disorder are discussed and the hypothesis, much favoured nowadays, of an anoxaemic origin is rejected. The author considers endocardial fibroelastosis to be a genetically determined malformation with excess formation of the endocardial fibroelastic component. *H. S. Baar*

16. **Morphological Changes in the Heart in Interstitial Plasma-cell Pneumonia.** (Morphologische Veränderungen am Herzen bei der interstitiellen, plasmazellulären Pneumonie)
A. GOEBEL and G. RUDOLPH. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **115**, 561–585, 1955. 9 figs., bibliography.

At the Pathological Institute of the University of Cologne 14 hearts from infants 2 to 5 months of age who died of interstitial plasma-cell pneumonia were examined histologically together with control specimens from the same age group. Pathological changes in the heart muscle were invariably found, consisting in: (1) interfibrillary oedema of the muscle fibres associated with disappearance of cross-striation, widening of the perinuclear zone, and sometimes with a fine granular disintegration of the whole muscle fibre; (2) comparatively rarely, perinuclear vacuolization, sometimes associated with nuclear hyperchromasia, the severest form of this type of change being represented by empty sarcolemma tubes; and (3) focally increased acidophilia, often associated with thickening and clumping of the myofibrils, which might finally disappear, a muscle fibre or part of it then staining uniformly deep black with Heidenhain's iron haematoxylin. In such fibres nuclear hyperchromasia was usually present, while sometimes the nucleus had disappeared, the fibre presenting the picture of coagulation necrosis. The myocardial changes were associated with endothelial swelling in the capillaries and arterioles and a watery imbibition of the whole wall. Similar changes were seen in the larger arteries of the heart and in veins. The pulmonary artery showed oedema of the wall and disintegration of its elastic fibres. The findings are compared with those in experimental anoxia, in beri-beri, and in potassium deficiency. The pathological changes in the myocardium and in the pulmonary artery in interstitial plasma-cell pneumonia are explained as being the result of anoxaemia due to the pulmonary changes and of pulmonary hypertension.
H. S. Baar

17. **Cell Types and Histologic Patterns in Carcinoma of the Lung. Observations on the Significance of Tumors Containing More Than One Type of Cell**
C. T. OLCOTT. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 975–995, Nov.–Dec., 1955. 10 figs., 30 refs.

This histological study is based on material collected over 28 years at the New York Hospital at necropsy on 234 patients (195 of them men) dying from carcinoma of the lung. On the average four blocks were cut from each lung tumour. The author distinguishes tumours composed of four different cell types: (1) a large, polygonal, anaplastic cell with abundant cytoplasm, not dissimilar in size and appearance to the cells of bronchial epithelium; (2) a small, round, anaplastic cell with hyperchromatic nucleus and very scanty cytoplasm; (3) squamous cells; and (4) columnar cells, this group including the so-called alveolar-cell carcinoma. In 76% of the cases the tumour had spread beyond the regional lymph nodes, the extent of spread being greatest in tumours with cells of Type 2. The average age at death was 58 years. With the single exception of a patient who survived 9 years after resection, the average survival time in the series was 6 months after onset of symptoms.

In 65% of the cases the tumour was composed of a single cell type; in 90 cases the cell was of Type 1 (polygonal cell group). Patients with the small round-cell tumours (Type 2) tended to have a more protracted clinical course, with an average survival time of 11 months, but the tumour metastasized widely, involving the liver in 7 of the 8 cases. Of the 38 cases of squamous-cell carcinoma, 8 showed pearl formation and only 5 (13%) metastasized to the liver, compared with 34% for the series as a whole. The columnar-cell tumours (Type 4) were characterized by their peripheral localization and the high proportion of female patients affected—18 out of 39 (47%), compared with 17% for all groups. In the remaining 83 cases the tumour consisted of more than

one cell type (usually two) in the primary focus or in the metastases or in both. It is worthy of note that where the two anaplastic cell types occurred together the smaller cell type was found in the centre and the larger at the periphery of the tumour, suggesting a relationship to active growth. Columnar-cell, squamous-cell, and large polygonal-cell tumours had metastasized in about two-thirds of the cases, but the small round-celled growths in 100%. The mixed types were transitional not only in their structure, but also in sex incidence, peripheral location, and metastatic rate. As the large polygonal cells appeared to merge with the small round cells, and also were found in close apposition to squamous and columnar cells, the author suggests that this cell type might be regarded as the basic cell of lung cancer, giving rise to all other cell types, and he stresses that this concept would lend support to the view that carcinoma of the lung is a single disease entity.

R. Salm

18. **Tuberculous Lesions Associated with Bronchial Cancer. A Morbid Anatomical Study.** (Les lésions tuberculeuses associées aux cancers bronchiques. Étude anatomique)

J. DELARUE and J. PAILLAS. *Presse médicale* [*Presse méd.*] **63**, 1788–1792, Dec. 25, 1955. 9 figs., 12 refs.

This is a study of 35 cases of bronchial carcinoma with concomitant tuberculosis, from the Laboratory of Pathological Anatomy of the Paris Faculty of Medicine. In 19 cases the lymph nodes only were affected, in one the bronchus, and in 15 the lung, the infection being in the pulmonary tissue related to the carcinomatous bronchus in 13 of these last, in 11 of which it was active. The authors point out the difficulty of distinguishing macroscopically between an excavating tumour mass and a tuberculous cavity. The frequency with which the tuberculosis was found in the related lobe is regarded as significant, as is also the frequency of occurrence of an active infection, especially in association with an anaplastic carcinoma.

A. C. Lendrum

19. **An Evaluation of the Concomitant Use of Cytological and Histocytological Techniques in the Recognition of Cancer in Exfoliated Material from Various Sources**

H. L. RICHARDSON, L. G. KOSS, and T. R. SIMON. *Cancer* [*Cancer (N.Y.)*] **8**, 948–950, Sept.–Oct., 1955. 6 refs.

The authors describe, from the Memorial Center for Cancer and Allied Diseases, New York, the results of a double method of examination of material submitted for diagnosis because of suspected cancer; this material included sputum, bronchial, nasotracheal, and oesophageal washings, and ascitic and pleural fluids. With the exception of the sputum, each fluid was centrifuged and (1) smears were made from the sediment for cytological examination, and (2) the residue was embedded in paraffin wax and sample sections cut and examined (the cell-block technique).

Out of a total of 4,017 specimens 2,613 were examined by both methods, and 578 of these were from cases considered on pathological and clinical grounds to be definitely cases of cancer. This diagnosis was confirmed by both methods of examination in 346 cases (60%), by smear alone in 164 (28%), and by cell-block examination alone in 68 cases (12%). The probable causes for a specimen being " negative " by smear and " positive " by cell-block examination are discussed. The authors express the opinion that carefully prepared smears are superior to the cell-block technique for diagnostic purposes because of the better preservation of cellular detail, but that the highest degree of accuracy will be achieved when both techniques are employed together.

R. J. Ludford

20. **Cytology of Esophageal Washings. Evaluation of 364 Cases**

W. D. JOHNSON, L. G. KOSS, G. N. PAPANICOLAOU, and J. F. SEYBOLT. *Cancer* [*Cancer (N.Y.)*] **8**, 951–957, Sept.–Oct., 1955. 11 figs., 16 refs.

The results of the cytological investigation of oesophageal washings from 364 patients are reported from the Memorial Center for Cancer and Allied Diseases, New York. Out of a total of 148 cases of primary malignant tumour of the oesophagus, cytological examination yielded a positive diagnosis of cancer in 103 (69·6%), another 18 cases (12·2%) being considered " suspicious ". Of 81 cases with oesophageal metastases (in the majority of cases from a primary gastric cancer), the results were positive in 25 and " suspicious " in 12. Of 135 cases in which no malignant growth was ever demonstrated, 3 were falsely diagnosed as positive and 7 as " suspicious ". A comparison of the results of cytological examination with those of biopsy in 148 cases of primary oesophageal cancer showed that the former were positive in 85 cases whereas the latter were positive in 117 cases; thus in 32 cases only biopsy gave a positive diagnosis, the results of cytological examination in these cases being negative or inconclusive.

In a few cases of severe chronic ulcerative oesophagitis of long standing abnormal epithelial cells were observed in smears. These cells were characterized by relatively large nuclei of irregular shape, with an atypical chromatin pattern, abnormal nucleoli, and cytoplasm which was often scanty and vacuolated. The presence of such cells in smears or sections constituted the chief source of diagnostic errors. It is not suggested that cytological examination can replace biopsy, but nevertheless it may prove of particular value in cases in which, for various reasons, biopsy is impracticable. Furthermore, the combined use of the two methods may occasionally eliminate the necessity for repeated oesophagoscopy.

R. J. Ludford

21. **The Pathology of Severe Digestion Oesophagitis**

P. M. PETERS. *Thorax* [*Thorax*] **10**, 269–286, Dec., 1955. 30 figs., bibliography.

Out of 20,000 cases in which necropsy was performed between 1930 and 1951, mostly at the Whittington Hospital, London, there were 116 cases of severe oesophagitis due directly to irritation by gastric juice. The condition affected patients of all ages and was slightly more frequent in males than females. Predisposing

factors present in 105 of the cases included one or more of the following: persistent vomiting and increased intra-abdominal pressure ("external factors"); acquired hiatal hernia, congenital enlargement of the hiatus and congenital shortness of the squamous oesophagus, mechanical interference with the crural tunnel, gastric ulcer or cancer ("internal factors"). Microscopically, the inflammation was non-specific in character and acute, chronic, or acute on chronic (implying repeated attacks); it was invariably associated with active or healed erosion or ulceration. Most damage occurred in the distal part of the oesophagus. Complications included haemorrhage, perforation, fibrous stricture, and leukoplakia. The incidence of the condition, for reasons not understood, is lower than might be expected. *A. Wynn Williams*

22. **Puncture Biopsy of the Liver in the Clinical Study of Internal Diseases.** (Цитологическое исследование печени в клинике внутренних болезней)
E. V. Chernȳsheva. *Терапевтический Архив* [*Ter. Arkh.*] **27**, 26–30, No. 8, 1955. 7 figs.

The author states that puncture biopsy of the liver, using a camphor needle as described by Abramov, is a safe and valuable procedure, enabling an accurate diagnosis to be made and providing a means of following the progress of the disease and its response to treatment. In a series of 200 punctures carried out on 165 patients suffering from various diseases of the liver, as well as conditions such as polycythaemia, leukaemia, and lymphogranulomatosis, it was possible to distinguish various types of hepatitis, cirrhosis, and pseudocirrhosis as well as primary tumours of the liver, and to classify the findings under the following ten headings.

(1) Acute and chronic epithelial hepatitis, acute and chronic mesenchymal hepatitis, and epithelial and mesenchymal cirrhosis. Acute epithelial hepatitis can be distinguished from acute mesenchymal hepatitis by the well-marked protein dystrophy of the hepatic cells, whereas the mesenchymal form exhibits as its predominant feature a hyperplasia of the reticulo-endothelial system. In the chronic forms, these same differences can be distinguished, although less clearly. In hepatic cirrhosis the large number of fibroblasts and collagenous fibres indicate the further progress of the disease; otherwise the appearances resemble those of the corresponding type of hepatitis.

(2) Cholangitis, pericholangitis, and biliary cirrhosis. It is possible to distinguish in the histological sections altered cells of the biliary ducts which as a rule are not visible in sections of puncture biopsy specimens in other types of hepatic disease. (3) Pigmented cirrhosis. The typical feature of biopsy specimens from livers affected by this type of disorder is the large amount of black pigment in and around the cells. Histochemical investigations reveal the large content of iron in the pigment. (4) In cases of pseudocirrhosis the sections present a distinctive picture, in which the main features are the relative absence of connective-tissue cells, changes in the capsular cells, and the presence of oedema.

(5) Subacute bacterial endocarditis, rheumatic heart disease, and atheromatous cardiosclerosis: the main features of this group of diseases are oedema of the liver, the slate-grey colour of the epithelial protoplasm, and the blurred contours of the hepatic cells. (6) Polycythaemia. Here the appearances are not typical; as a rule protein dystrophy is present, but there is seldom any evidence of cirrhosis. (7) Leucoses. It is easy to distinguish true leucoses from leukaemoid reactions by the presence of foci of haematopoietic tissue; but in leukaemic lymphadenosis the picture is not so clear, and such foci are not found in cases of this type. (8) Lymphogranulomatosis. In this disease the cell picture is polymorphic and similar to that found in lymph nodes from such cases. If Sternberg cells can be demonstrated the diagnosis is conclusive. (9) In 23 out of 29 cases of blastomatosis the microscopic picture was clearly diagnostic. The author states it is easy to recognize neoplastic tissue if the puncture is made into a nodule; but it is important to distinguish hyperplasia of reticulo-endothelial tissue from a neoplastic process. The exact nature of metastatic tumours is often difficult, and sometimes impossible, to define. (10) Among the other diseases recognized were abscess of the liver, one case of Gaucher's disease, and one of Down's disease.

The article is illustrated with one monochrome and six coloured photomicrographs. *L. Firman-Edwards*

23. **Biopsy of the Rectum in Ulcerative Colitis**
G. Lumb and R. H. B. Protheroe. *Lancet* [*Lancet*] **2**, 1208–1215, Dec. 10, 1955. 18 figs., 26 refs.

The histological changes seen in 180 rectal biopsy specimens from 150 patients with ulcerative colitis are described in this paper from the Westminster Hospital, London; 100 similar specimens from patients whose rectal mucosa was normal were used for purposes of comparison. Each specimen was taken under direct vision with Officer's forceps through a sigmoidoscope and without anaesthesia at a level of 11 cm. from the anal sphincter, bisected, and placed in Susa fixative for 12 hours. Histological sections 5 μ thick were stained with Weigert's haematoxylin and azo-eosin. Healing of normal rectal mucosa after deliberate minor surgical injury was also studied. The microscopical appearances of the rectal mucosa in ulcerative colitis are non-specific in character. In 13 cases (8·7%) the mucosa was normal; in the remaining 137 (91·3%) there were lesions of varying severity. "Crypt abscesses" were prominent in the early stages of the disease; these might be limited or might spread, with extensive erosion and ulceration. The number of polymorphonuclear leucocytes, lymphocytes, and plasma cells varied considerably, but often increased with the age of the lesions. In healed lesions goblet cells were numerous, but the rectal mucosa was thin and fibrosed and contained only few glands. Histological recognition of the disease in its quiescent phase—that is, in the absence of erosion or ulceration—is thus possible, as was the case in 48 out of the 180 specimens in this series. The pathogenesis of ulcerative colitis is still not known, but the authors suggest that failure of normal regeneration of intestinal epithelium may be important. *A. Wynn Williams*

Pharmacology

24. The Effects of Reserpine and Chlorpromazine on Gastric Secretion

B. J. HAVERBACK, T. D. STEVENSON, A. SJOERDSMA, and L. L. TERRY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 601–604, Dec., 1955. 3 figs., 6 refs.

Reserpine administered orally and intravenously has been shown to increase the volume and free acidity of gastric secretion. Chlorpromazine reduced the volume of gastric secretion but did not significantly change the free acidity. Chlorpromazine would appear to be the tranquillizing agent of choice when stimulation of gastric secretion is contraindicated.—[Authors' summary.]

25. Clinical Evaluation of Diuretic Mersoben

R. H. CHANEY and R. F. MARONDE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 26–29, Jan., 1956. 5 refs.

In the search for an effective mercurial diuretic of minimal toxicity and greater potency the authors have tried the effect of " mersoben ", an aliphatic compound, 3-(2-hydroxy-3[-D-gluco-pentahydroxyhexyl-mercapto-mercuri]-propyl)-D-mannitol. At the County General Hospital, Los Angeles, the drug was given intramuscularly to 85 patients with cardiac failure in doses of 175 or 140 mg., these doses being calculated to contain 50 and 40 mg. of mercury respectively. The efficacy of the diuretic was judged by the loss of weight which occurred in the 24 hours following the injection.

The diuretic was found to be potent and to cause no ill effects, except infrequently some slight pain at the site of injection. Its low content of mercury is thought to be an advantage. *G. S. Crockett*

26. Effect of Intravenous Vitamin K_1 on the Action of Phenindione

P. DAWSON. *British Medical Journal* [*Brit. med. J.*] 2, 1427–1429, Dec. 10, 1955. 5 figs., 13 refs.

The effect of intravenous administration of an emulsion of vitamin K_1 on human subjects receiving phenindione was studied at St. George's Hospital, London. The subjects received phenindione for 4 days, by which time the prothrombin activity was of the order of 10 to 20%. A single intravenous injection of the emulsion of vitamin K_1 was then given and the prothrombin activity estimated at varying intervals. The subjects continued to take phenindione until the end of the investigation.

In 10 subjects given either 10 or 20 mg. of vitamin K_1 the prothrombin activity rose to 100% within 24 hours; in 14 others given 5 mg. the prothrombin activity rose to a maximum of 50 to 100% in 6 to 24 hours. An appreciable rise in prothrombin activity was observed within 3 hours of injection of vitamin K_1 in 12 out of 19 subjects. There was no evidence that the increase in activity was more rapid in those who received 20 mg. than in those who received 5 mg. In 2 volunteers who were given 5 mg. of the vitamin emulsion there was still a slight elevation of the prothrombin activity 72 hours later, while in 3 others activity had fallen below 20% between 48 and 72 hours later. In 4 subjects the prothrombin value determined by the globulin assay technique was moderately reduced (33 to 50%), but was raised to 100% within 6 hours of administration of vitamin K_1. A control group of 5 subjects who did not receive vitamin K_1 discontinued phenindione therapy; in one of these the prothrombin activity rose to normal within 48 hours, and in the other 4 it was normal within 72 hours. No toxic effects were observed after 40 intravenous injections of the emulsion of vitamin K_1.

The author suggests that 5 mg. of this preparation is sufficient to raise a dangerously low level of prothrombin activity in a subject receiving phenindione, and that 10 to 20 mg. is adequate for the treatment of haemorrhage resulting from administration of the latter drug.

Charles Rolland

27. Phenylpropyl-hydroxycoumarin as an Anticoagulant

M. TOOHEY. *British Medical Journal* [*Brit. med. J.*] 1, 9–11, Jan. 7, 1956. 8 refs.

Phenylpropyl-hydroxycoumarin (" marcoumar ") was administered at New End Hospital, London, to 104 patients, most of whom were suffering from coronary thrombosis or phlebothrombosis. The optimum initial dose in most cases was 24 mg., but in young, robust, and less acutely ill patients this could with advantage be increased to 27 to 30 mg. The second dose depended upon the prothrombin time 24 to 36 hours after the initial dose, and varied from 3 to 15 mg. The prothrombin time was determined by Quick's one-stage method with human brain thromboplastin, prothrombin levels of between 10 and 20% or a prothrombin time two to three times the normal being aimed at. Quick's test was performed daily for the first 6 or 7 days, then 3 times a week for at least 2 weeks.

A satisfactory therapeutic prothrombin time was attained in 48 hours in 29 out of 35 patients given 24 mg. initially. The daily maintenance dose varied from 0·75 to 6 mg.; 80 patients (out of 99) required 1·5 to 4·5 mg. It was necessary frequently to adjust the maintenance dose because an error in dosage as small as 0·5 mg. a day for a few days was sufficient to cause considerable alteration in the prothrombin time.

Response to the drug varied and, as with other anticoagulants, smaller doses were required by older patients, those who were underweight, were seriously ill, or had hepatic or renal disease. The author states that in 10% of cases there was an unforeseen and unpredictable rise of the prothrombin time above 60 seconds. The drug has a prolonged cumulative action, and after it was

withdrawn it usually took 4 to 5 days for the prothrombin time to rise from the therapeutic range to 50% and more in the presence of hepatic or renal dysfunction. Haematuria occurred in 5 patients, but was macroscopic in only one. Vitamin K_1 in a dosage of 5 to 15 mg. by mouth was an effective antidote, and if the prothrombin time exceeded 90 seconds this dose was repeated. Parenteral administration of the vitamin was necessary only if haemorrhage was severe and the prothrombin time markedly prolonged.

[This is rather an unfavourable report on the drug.]

T. B. Begg

28. A Comparison of the Hypnotic Effects of Chloral and Ethinamate

E. L. FOLTZ, F. DRACOS, and C. M. GRUBER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 528–535, Nov., 1955. 2 figs., 12 refs.

The efficacy of a new non-barbiturate hypnotic, L-ethinyl-*cyclo*-hexylcarbamate (" ethinamate "), was compared with that of chloral alcoholate in 10 patients at the University of Pennsylvania School of Medicine. Capsules containing 1 g., 1·5 g., or 2 g. of either chloral alcoholate or ethinamate were given at bedtime and the effects of the drugs on blood pressure, pulse and respiration rates, and the degree of central nervous system depression were estimated at intervals throughout the night. Neither the patients nor the observers knew which drug was being given. Statistical analysis showed that 1·4 g. of ethinamate produced the same degree of central nervous depression as 2 g. of chloral alcoholate; moreover, gramme for gramme, ethinamate had a longer duration of action than chloral. To assess the subjective effects of the drugs 51 patients who were moderately ill received capsules containing chloral alcoholate, ethinamate, or a placebo, the doses of the active drugs being 0·5 g. in some cases and 1 g. in others; in this investigation a " double-blind cross-over " procedure was employed. Questioning of the patients revealed that there was a small but significant increase in the number who reported an improvement in the quality of sleep, with an earlier onset, when ethinamate was given; moreover, side-effects were found to be less frequent after ethinamate than after chloral alcoholate.

Bernard Isaacs

29. The Action of Analgesics and Nalorphine on the Cough Reflex

A. F. GREEN and N. B. WARD. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 418–423, Dec., 1955. 2 figs., 16 refs.

The antitussive properties of morphine, codeine, pethidine, amidone, piperidylamidone, thiambutene, pholcodine, narcotine, and nalorphine were studied at the Wellcome Research Laboratories, Beckenham, Kent. In animals lightly anaesthetized with pentobarbitone sodium a cough reflex was induced in one of three ways: (1) by electrical stimulation of the central end of the cut superior laryngeal nerve, which produced a series of inspiratory gasps; (2) by introduction of an intratracheal tube; or (3) by insufflation of sulphur dioxide.

Amidone was the most powerful suppressant of coughs caused by electrical stimulation in cats, having eight times the antitussive effect of morphine, twenty times that of pethidine, and eighty times that of codeine. The antitussive effect of drugs possessing analgesic properties was proportional to their morphine-like action; morphine had the greatest and pethidine the least depressing effect on respiration. As a cough depressant pholcodine was slightly more effective than codeine, while narcotine was relatively ineffective. Nalorphine, which had no effect alone, abolished the action of morphine and allied compounds, including codeine, but not that of either pholcodine or narcotine, suggesting that the mode of action of these last drugs is different. Experimental results are described in detail and discussed with reference to other published work.

Kenneth Gurling

30. Effectiveness of Salicylamide as an Analgesic and Antirheumatic Agent. Evaluation of the Double Blindfold Technique for Studying Analgesic Drugs

R. C. BATTERMAN and A. J. GROSSMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1619–1622, Dec. 24, 1955. 17 refs.

From Flower and Fifth Avenue Hospitals (New York Medical College), New York, the authors report the results of a clinical comparison of aspirin, a placebo, and salicylamide in the treatment of 73 out-patients with painful arthritic conditions. The double-blind technique was used, the dose of each drug was 0·6 g. every 4 hours, and assessment of the results was based on subjective reports. All results were subjected to statistical analysis.

The over-all efficacy (the criteria of which are defined) appeared to be about 60% for each drug. Mild untoward reactions were noted in 25% of those given aspirin, in 17% of those given the placebo, and in 31% of those receiving salicylamide. Asked to state a preference for one medicament, the patients showed a tendency to prefer the placebo. In a further test, of 46 in-patients, effective analgesia was obtained in 60% with aspirin, in 47% with the placebo, and in 27% with salicylamide. A statistically significant number of these patients preferred aspirin to salicylamide.

Details are also given of a similar study carried out on 57 patients in which salicylamide, N-acetyl-*p*-aminophenol, and a placebo were compared. The results were similar to those in the first trial. The administration of salicylamide to 20 ambulatory arthritic patients resulted in satisfactory analgesia in only 15%.

In view of these conflicting and surprising results, the authors express doubt about the value of the double-blind technique in the assessment of drugs in chronic ailments, suggesting that this method results in a levelling-off of incidence of effectiveness, so that active drugs may be erroneously condemned as ineffective because the same response is obtained with a placebo.

[This challenge to the validity of the double-blind technique in therapeutic trials is important, and the arguments set out in the original paper are worthy of study.]

T. J. Thomson

Chemotherapy

31 (*a*). **A Trial of Actinomycin C in the Treatment of Malignant Lymphadenopathies.** (Essai de l'actinomycine C dans le traitement des adénopathies malignes)
P. CROIZAT and G. LACOSTE. *Presse médicale* [*Presse méd.*] 63, 1681, Dec. 3, 1955. 1 ref.

31 (*b*). **Fatal Agranulocytosis from Treatment with Actinomycin C in High Dosage.** (Agranulocytoses mortelles par traitement à doses fortes d'actinomycine C)
M. JANBON, L. BERTRAND, and G. CARLI. *Presse médicale* [*Presse méd.*] 63, 1682–1683, Dec. 3, 1955. 2 figs., 8 refs.

31 (*c*). **Further Observations on the Treatment of Malignant Blood Diseases with Actinomycin C.** (Nouvelles remarques sur le traitement des hémopathies malignes par l'actinomycine C)
J. OLMER. *Presse médicale* [*Presse méd.*] 63, 1683, Dec. 3, 1955. 1 ref.

31 (*d*). **Results of the Therapeutic Use of Actinomycin C.** (Résultats de l'emploi de l'actinomycine C en thérapeutique)
J. TAPIE. *Presse médicale* [*Presse méd.*] 63, 1684, Dec. 3, 1955.

31 (*e*). **Indications for the Use of Actinomycin C in Tumours of the Reticuloendothelial System.** (A propos des indications de l'actinomycine C dans les tumeurs du système réticulaire)
R. GILBERT and E. THOMMEN. *Presse médicale* [*Presse méd.*] 63, 1685, Dec. 3, 1955. 1 ref.

31 (*f*). **Further Clinical Studies on the Action of Actinomycin C.** (Nouvelles études cliniques sur l'action de l'actinomycine C)
A. RAVINA and M. PESTEL. *Presse médicale* [*Presse méd.*] 63, 1686–1687, Dec. 3, 1955.

Clinical trials of actinomycin C in the treatment of malignant disease were started in March, 1954, under the auspices of the Ministry of Public Health, in several centres in France, and the preliminary results formed the subject of a symposium published in May, 1954 (*Presse méd.*, 1954, **62**, 737; *Abstracts of World Medicine*, 1954, **16**, 369). Further results are now reported. The antibiotic was given intravenously, the dose being progressively increased from 100 μg. to about 600 μg. daily, up to a total of 1 to 12 mg. The main toxic effects were stomatitis, diarrhoea and vomiting, alopecia, and jaundice, but they disappeared when the drug was discontinued. Different batches of actinomycin appeared to vary in their toxic effects. Janbon *et al.*, writing from the Regional Hospital Centre of Montpellier, warn against giving high doses, 2 patients to whom they gave 1,000 μg. daily for about 2 weeks having died with stomatitis, granulopenia, and severe diarrhoea.

The general conclusions reached are as follows. About half of the patients with Hodgkin's disease may improve under treatment with actinomycin C, with fall of temperature, increased appetite, and a decrease in size of the peripheral lymph nodes. The remissions are only temporary, however, and are usually inferior to those obtained with nitrogen mustard or radiotherapy, although the drug may be of value as a supplement to these forms of treatment. In other types of malignant disease the results are disappointing. Ravina and Pestel, at the Hôpital Beaujon, Clichy, are again rather more optimistic than their colleagues, although they have now abandoned the high doses which they used previously. They claim to have obtained relief not only in Hodgkin's disease, but also in certain cases of leukaemia and cancer [but since they report only selected favourable cases, their over-all results cannot be assessed].

P. C. Reynell

32. **Studies on Analogues of L-Cysteine and L-Cystine. I. Some Structural Requirements for Inhibiting the Incorporation of Radioactive L-Cystine by Leukemic Leukocytes. II. The Effect of Selenium Cystine on Murphy Lymphosarcoma Tumor Cells in the Rat. III. The Effect of Selenium Cystine on Leukemia**
A. S. WEISBERGER, L. G. SUHRLAND, and J. SEIFTER. *Blood* [*Blood*] **11**, 1–10, 11–18, and 19–30, Jan., 1956. 7 figs., 29 refs.

There is some evidence that the sulphur-containing amino-acid L-cysteine (which for metabolic purposes may be regarded as identical with L-cystine) is important in the metabolism of leucocytes, since leucopenia develops in animals fed on a diet deficient in L-cystine. The leucocytes in acute leukaemia and chronic myeloid leukaemia show a more rapid turnover of radioactive L-cystine than normal leucocytes, and may therefore be readily affected by substances which reduce the availability of L-cystine or L-cysteine.

This possibility was studied at Western University School of Medicine, Cleveland, Ohio, by measuring the rate of influx of radioactive L-cystine into leukaemic leucocytes which had previously been incubated with L-cysteine, D-cysteine, or derivatives in which the sulphydryl, amino, or carboxyl groups had been modified or substituted. With cells incubated with increasing concentrations of unlabelled L-cysteine there was a progressive decrease in the amount of radioactive L-cystine incorporated, but incubation with D-cysteine was without effect. Of the many derivatives of L-cysteine tested, only 3—L-selenium cystine, D-selenium cystine, and phenyl selenium cysteine—were found to decrease the intake of radioactive L-cystine at low concentrations.

In the second part of the paper a study of the effect of selenium cystine on the influx of radioactive L-cystine into rat lymphosarcoma cells *in vitro* and *in vivo* and also on the rate of growth of the tumour *in vivo* is reported. The rate of incorporation of radioactive L-cystine into a suspension of homogenized tumour tissue in serum in

the presence of selenium cystine was only 29% of the control value. Benzyl selenium cysteine was tested similarly, but was without effect. Radioactive L-cystine injected intraperitoneally into tumour-bearing rats was rapidly distributed to the liver, kidney, spleen, and tumour, the tumour containing the smallest amount. When selenium cystine was given orally one hour before administration of the radioactive cystine, the uptake of the latter by tumour tissue fell considerably and an increased amount was deposited in the liver. The rate of growth of transplanted tumours was reduced in rats treated with selenium cystine, and regression occurred in a higher proportion of cases. The mechanism of this effect of selenium cystine is not known, but the observation that benzyl selenium cysteine was again ineffective suggests that the decrease in tumour growth is related to the ability to reduce the availability of L-cystine and shows that it is unrelated to the presence of selenium.

In the third part of the paper the effects of selenium cystine on patients with acute and chronic leukaemia are reported. The drug was given by mouth to 4 patients, 2 with acute leukaemia and 2 with chronic myeloid leukaemia, doses of 100 mg. daily being administered for 10 to 57 days. In all cases the total leucocyte count fell rapidly and the spleen became smaller, even in patients refractory to other therapeutic agents. Toxic effects included severe nausea, vomiting, and anorexia, with severe alopecia and marked destruction of the nail-beds. There was no impairment of hepatic or renal function even after prolonged administration of the drug, and post-mortem examination of 2 patients revealed no toxic changes. On account of these effects only a limited period of treatment was permissible and the possibility of obtaining an appreciable remission of the disease could not be determined. Full case reports are given and laboratory findings described.

H. G. Crabtree

33. Sensitivity of Four Species of *Bacteroides* to Antibiotics

L. P. GARROD. *British Medical Journal* [*Brit. med. J.*] 2, 1529–1531, Dec. 24, 1955. 15 refs.

Previous reports on the sensitivity to antibiotics of microorganisms of the *Bacteroides* group have been vague both in regard to the true identity of the organism tested and the concentrations of antibiotic which were effective. This paper from St. Bartholomew's Hospital, London, reports in detail the findings with 23 strains of *Bacteroides fragilis*, 6 of *B. fusiformis*, 4 of *B. necrophorus* (*funduliformis*), and 22 of *B. melaningogenicum*, all of which were tested against the nine antibiotics, penicillin, streptomycin, chloramphenicol, oxytetracycline, erythromycin, polymyxin, and bacitracin on poured plates containing the appropriate antibiotic in concentrations ranging from 16 to 0·007 μg. per ml.

Streptomycin was shown to be the least satisfactory antibiotic for all 4 species. Only *B. fragilis* was resistant to penicillin, while *B. melaninogenicum* (which is commonly associated with sepsis in abdominal wounds and in the uterus) was very sensitive to penicillin. The most active antibiotic against *B. fragilis* was tetracycline. Erythromycin and bacitracin were only moderately active against *B. melaninogenicum*, but only *B. fragilis* was resistant to polymyxin. The author suggests that these findings are important as indicating the best type of therapy to be used in a particular case; for example, as several days are required to isolate, culture, and determine the sensitivity of organisms in this group the frequent association of *B. fragilis* with lower-bowel lesions would suggest the immediate use of tetracycline in such cases. Penicillin would be the choice in most other infections except mixed ones, in which case the choice will depend on the sensitivity of any other bacteria that may be present.

R. F. Jennison

34. Antibiotics in Experimental Tetanus: *in vitro* and *in vivo* Studies

A. A. ANWAR and T. B. TURNER. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] 98, 85–101, Feb., 1956. 16 refs.

35. Recent Studies on Albomycin, a New Antibiotic

G. F. GAUSE. *British Medical Journal* [*Brit. med. J.*] 2, 1177–1179, Nov. 12, 1955. 3 figs., 16 refs.

The author describes some recent studies carried out on albomycin at the Institute for Antibiotic Research (Academy of Medical Sciences), Moscow. Albomycin, a cyclic iron-containing peptide, was first isolated by the author with Brazhnikova in 1951 from cultures of the streptomycete *Actinomyces subtropicus*. It strongly inhibits the growth of a variety of Gram-negative and Gram-positive organisms, and is particularly effective *in vitro* and *in vivo* against staphylococci which have proved resistant to other antibiotics. The pure drug has been shown to be about ten times more potent than penicillin. It forms a reversible complex with serum proteins and is non-toxic in animals and man after subcutaneous, intravenous, and intrathecal injection. It has proved effective in the treatment of pneumonia and, given intrathecally, of pneumococcal meningitis, particularly in children; it has also been of value in a variety of surgical infections and in cases of prostatitis and gonococcal urethritis resistant to penicillin.

F. W. Chattaway

36. Penicillin V: Further Observations

W. J. MARTIN, D. R. NICHOLS, and F. R. HEILMAN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] 30, 521–526, Nov. 2, 1955. 2 refs.

The authors have investigated, at the Mayo Clinic, the diffusion into various body fluids and tissues and the concentration in the serum of penicillin V (phenoxymethyl penicillin) when administered orally in doses up to 1,000,000 units. The antibiotic was shown to be readily absorbed and to diffuse into ascitic and pleural fluids and thyroid tissue, but not into the cerebrospinal fluid in the absence of meningeal inflammation. It was found that when it was given together with probenecid the serum level of the antibiotic after 2 hours was higher than when it was given alone. Penicillin V is concentrated in the liver and excreted in the bile in a biologically active form. Details of the concentration of the drug in the various tissues investigated are given in a series of tables.

F. W. Chattaway

Infectious Diseases

37. Tissue Culture Isolation of Coxsackie Group B Viruses in Aseptic Meningitis

W. M. M. KIRBY and C. A. EVANS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 743–746, Oct. 22, 1955. 10 refs.

An investigation is reported of 66 cases of poliomyelitis admitted to King County Hospital, Seattle, between July and December, 1954, in some of which there was infection with Coxsackie Group B viruses. Specimens of stool from each case were suspended in distilled water and the supernatant was used for inoculation of trypsinized monolayer cultures of kidney tissue from rhesus monkeys. Altogether 51 strains of virus were isolated from these 66 cases, most of them being strains of poliomyelitis virus. In 14 instances, however, the strains caused a slow, patchy degeneration of the monkey kidney tissue and were not neutralized by poliomyelitis antisera; neutralization tests showed that 13 of these were of Coxsackie B-2 virus and one was of Coxsackie B-4 virus. Of the 14 patients with Coxsackie virus infection, 13 had non-paralytic poliomyelitis; in the remaining case, with paralysis, poliomyelitis virus was isolated from the stools subsequently. In all cases serum neutralization tests confirmed the presence of Coxsackie virus infection, but there was no conclusive serological evidence of recent infection with poliomyelitis virus; in several of the patients poliomyelitis antibodies were present only in low titre. Features of the Coxsackie infection were fever, stiff neck, and pleocytosis, but in 8 of the cases the cerebrospinal fluid contained less than 100 cells per c.mm. No difference was observed clinically between patients with Coxsackie virus infection and those without paralysis from whom poliomyelitis virus was isolated. *D. G. ff. Edward*

38. Production of Pharyngoconjunctival Fever in Human Volunteers Inoculated with APC Viruses

T. G. WARD, R. J. HUEBNER, W. P. ROWE, R. W. RYAN, and J. A. BELL. *Science* [*Science*] **122**, 1086–1087, Dec. 2, 1955. 8 refs.

Acute catarrhal conjunctivitis was produced in a number of volunteers by inoculation on the conjunctival and pharyngeal mucosa of fluid containing virus isolated from patients with acute respiratory disease. One group of 20 subjects received adenoidal–pharyngeal–conjunctival (A.P.C.) Type-4 virus (RI-67) from the third passage through monkey kidney tissue cultures. Of another group of 20 subjects, 7 received a mixture of approximately equal parts of virus-containing throat washings from a patient with sore throat and fever and fluid from the sixth passage through monkey kidney tissue cultures of a virus of A.P.C. Type 3, which was recovered from a case of pharyngo-conjunctival fever; the remaining 13 received pooled material containing virus obtained during the same outbreak.

Of the 40 subjects, 26 developed catarrhal conjunctivitis in the inoculated eye after an incubation period of 2 to 7 days, this being accompanied by sore throat in 20, cough in 15, headache in 13, nasal symptoms in 25, and febrile symptoms in a few. Usually the illness lasted 7 to 10 days. Control inoculum applied to the other conjunctival sac in each volunteer had no visible effect. Neutralizing antibody tests showed that usually where illness developed there was a low initial antibody titre and a fourfold or greater rise in titre at the third or fourth week. The virus was recovered from eye or throat swabs in a high proportion of cases.

[Koch's postulates have now been sufficiently fulfilled to prove that some cases of acute respiratory disease are caused by viruses of the A.P.C. group.]

G. C. R. Morris

39. On the Question of Pathogenesis of Influenza. (К вопросу о патогенезе гриппа)

F. G. ÉPSHTEÍN. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 68–74, No. 1, 1956. 25 refs.

In this communication from the Influenza Clinic of the Ivanovski Institute of Virology, Moscow, the author expresses his disagreement with Burnet's theory of the pathogenesis of influenza. He then reviews the experimental work on influenza published in the Soviet Union, and on the basis of this and the teachings of Botkin and Pavlov, he proffers his own concept. He considers that the toxic substances produced by the living virus, or possibly the virus particles themselves, cause irritation of the vagal sensory endings in the mucosa of the respiratory tract, where the virus first settles. These irritating impulses travel to the cortex of the brain where they interfere with cortical control of the defence reactions.

From the cortex the influence spreads to the lower centres and to the autonomic ganglia and nerves, through which cortical and subcortical control over the whole organism is exercised. In adults predominantly parasympathetic stimulation results; this leads to dilatation of blood vessels which causes the appearance of hyperaemia and blotchiness of the face, injection of the mucosa of the nose, mouth, larynx, trachea, and bronchi, hypotension, bradycardia, excessive perspiration, dermatographia, an increase in mucus secretion, and leucopenia. At the same time the functional changes in the brain are associated with physical signs such as hyperaemia, oedema, perivascular infiltration, and degenerative changes in the cells of the ganglia. The irritation of the epithelial vagal receptors produces reflex dystrophic alterations in the cells already damaged by the virus, causing their further disintegration and thus allowing the spread of the virus. In addition, the presence of the virus in the body is associated with the circulation of certain toxic substances the nature of which is not known with certainty. These irritate sensory nerve endings in

the blood vessels, from which in turn noxious influences are transmitted to the central nervous system. Finally, the damage to the epithelium of the respiratory passages, together with the impairment of the defence mechanisms, allows multiplication of secondary invaders and the development of complications. *Marcel Malden*

40 (*a*). **Practical Trial of Antirabies Serum in Persons Bitten by a Rabid Wolf.** (Essai pratique du sérum antirabique chez les mordus par loups enragés)
M. BALTAZARD and M. BAHMANYAR. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **13**, 747–772, 1955. 12 figs., 5 refs.

40 (*b*). **Laboratory Data Supporting the Clinical Trial of Antirabies Serum in Persons Bitten by a Rabid Wolf**
K. HABEL and H. KOPROWSKI. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **13**, 773–779, 1955.

In recent years the results of the classic prophylactic vaccine treatment of persons bitten by rabid wolves in Iran have been poor. In view of the favourable results obtained with hyperimmune serum in experimental animals, the Expert Committee on Rabies recommended to the Executive Board of the World Health Organization in 1950 that an evaluation of this method of treatment be undertaken in man, and the Pasteur Institute of Iran was chosen for this purpose. Isolated cases were treated successfully, but it was not until August, 1954, that the opportunity arose for a decisive test when a rabid wolf bit 29 persons and all but 2 were treated within 32 hours. The clinical and laboratory findings are described in two papers, the first from the Pasteur Institute at Teheran and the second by two members of the W.H.O. Expert Committee on Rabies. [The two papers should be read together and in full. Both are of great importance.]

The victims were inhabitants of a village 500 km. from Teheran who were attacked by a large wolf (subsequently proved to be rabid by isolation of the virus and identification of Negri bodies) which in the course of 5 hours bit no fewer than 29 men, women, and children and at least 3 cows, fought a dog, and attacked a horse whose owner finally killed it. The raid started at about 1 a.m. and many of the victims were attacked while sleeping out of doors because of the heat. As a result 18 were bitten on the head, some having bites on the body or limbs as well. The authors state that the mortality in such cases hitherto has been more than 40%. Many of the injuries were very severe—one boy aged 6 years actually had his skull fractured and the dura mater torn, so that he literally received an intracranial inoculation of virus. After first-aid treatment at the village hospital, 27 of those bitten were sent, together with the wolf's head, by truck to Teheran, which they reached after 23 hours, while the 2 others arrived some days later.

Of the 18 patients with head wounds, 17 (that is, all but the boy of 6) were divided into three groups and treated as follows: (A) 5 patients received a standard course of vaccine and 2 injections of serum (on the 1st and 5th days); (B) 7 patients received vaccine and one injection of serum (on the 1st day); and (C) 5 patients received vaccine only. The 11 patients bitten on the trunk or limbs only were divided into two groups and treated as follows: (D) 4 patients received vaccine and one injection of serum (on the 1st day); and (E) 7 patients received vaccine only. The vaccine used was a 5% phenolized emulsion of sheep brain, 5 ml. of which was given subcutaneously into the abdominal wall daily for 21 days. The serum was prepared in rabbits and doses of approximately 0·65 ml. per kg. body weight injected intramuscularly to a maximum of 50 ml. The little boy (who recovered) was given vaccine daily for 20 days and 20 ml. of serum every other day for 6 doses, with penicillin for the secondary infection of the meninges.

Of the 29 patients, 4 died—one in Group B on the 22nd day, and 3 in Group C on the 31st, 32nd, and 62nd days respectively after being bitten. There were no deaths in Groups A, D, and E. The survivors have been kept under observation for 12 months since the attack.

In the second paper details are given of the antibody levels in samples of blood taken daily until the 14th day of treatment, then every other day until the 22nd day, and then every 4th day until the 54th day. [For technical details the original paper should be consulted.] In Groups A and B antibody was definitely detected in the blood during the first 5 days after starting treatment, whereas in Group C no antibody was present before the 19th day in any case, while none at all was detected throughout the period of observation in 2 cases (one of which was fatal, the injuries in the other being superficial only). In the one fatal case in Group B only a trace of antibody was found in the blood after the 7th day, whereas in the other cases in this group the level was maintained until the 21st day after 2 injections of serum, but fell markedly after a single dose.

[Although these results are not absolutely conclusive, it does seem likely that the serum played an important part in bringing about the happy outcome in Groups A and B, in which the injuries (some of which are shown in excellent photographs) were such that no one would have dared to give more than the most guarded prognosis, especially for the little boy. However, it would be advisable to keep the patients under observation for at least another year as the abstracter knows of a fully authenticated case in which the patient died from rabies 365 days after being bitten, while Babés has reported a case in which he was satisfied that the incubation period was 2 years.] *W. K. Dunscombe*

41. **Tetracycline in the Treatment of Brucellosis.** (La tetraciclina nella terapia della brucellosi)
F. CONTI, A. CASSANO, G. MIANO, M. MAZZEO, and R. BARLETTA. *Aggiornamenti sulle malattie da infezione* [*Aggiorn. Mal. Infez.*] 1, 359–374, Nov.–Dec., 1955. 23 refs.

The authors report from the Institute of Medical Pathology, University of Rome, their experience with tetracycline in the treatment of 10 cases of brucellosis, of which 9 were due to infection with *Brucella melitensis* and one with *Br. abortus*. The antibiotic was given in doses of 250 mg. every 3 hours—reduced after a few days to 250 mg. 6-hourly—either alone or in association with

the intravenous injection of a vaccine. In 8 cases the temperature began to fall between the 4th and 6th days, but in 2 the fever persisted for 2 weeks. Altogether 7 patients responded favourably to tetracycline, of whom 2, however, had a relapse and recovered only after a second course of treatment. The combined treatment was given in 5 cases and was successful in all but one in which neither the antibiotic nor the vaccine therapy had any effect upon the infection. *Franz Heimann*

42. Results of a New Method of Treatment for Scarlet Fever. (Ergebnisse einer neuen Behandlungsmethode des Scharlach)

J. PROCHÁZKA and V. KREDBA. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 145–147, Feb. 11, 1956. 15 refs.

During the period 1938–54 the authors treated 57,392 cases of scarlet fever at the Clinic for Infectious Diseases, Prague, 86·3% of these being in children under 14 years.

The cases fall into two groups. From 1938 to the end of May, 1949, 26,600 cases were treated with sulphonamides (0·15 g. per kg. body weight) for 5 to 7 days, the more severe cases also being given convalescent serum or plasma, while from 1947 complications were treated with penicillin as well. Patients were hospitalized for 6 weeks to 3 months, depending on complications. The mortality in this group was 0·4%, the majority of the deaths being from sepsis and pneumonia. (Before the advent of penicillin the mortality was 1%.) The complication rate was 21·2%.

From June, 1949, onwards 30,732 cases were treated by what the authors regard as a new method, daily injections of 200,000 to 500,000 units of procaine penicillin being given for 5 days. (In some cases penicillin tablets were given by mouth in double this dosage.) In severe toxic cases the dose by injection was increased to 1 mega unit, plasma transfusion being given as well. In the average case the patient was kept in hospital for 5 days, mainly to simplify giving the penicillin injections, and was nursed in a small 5-bedded ward. To prevent superinfection new admissions were kept apart from patients already under treatment, the patient becoming non-infectious within 24 or 48 hours of starting treatment. Daily concurrent disinfection of the ward was carried out, and the nursing staff wore masks and were examined regularly for the carrier state. After 5 days in uncomplicated cases the patient was sent home by special ambulance and remained isolated there for a further 14 days, the first week being spent in bed, the second convalescent. Provided no abnormality was present on examination after this period the patient was allowed to return to school or to work. Among the patients so treated there were no deaths, while the incidence of complications varied from 2 to 7%, those occurring at home being so mild as not to require further hospitalization and the majority taking the form of enlargement of the submandibular lymph nodes. Whereas in 99% of cases throat swabs were positive for β-haemolytic streptococci, on discharge the proportion was 0·25%. On the other hand an increase in the relapse rate from 7 to 12% occurred during this second period, which the authors can attribute only to the recent tendency for several types of streptococcus to be present during an epidemic, instead of a single predominant type as in the past.

I. M. Librach

43. Moniliasis Treated with Pentamidine

A. STENDERUP, J. BICHEL, and F. KISSMEYER-NIELSEN. *Lancet* [*Lancet*] **1**, 20–21, Jan. 7, 1956. 1 fig., 2 refs.

The results in 3 cases (in one patient with chronic myeloid leukaemia and 2 with Hodgkin's disease) of severe monilial infections of the respiratory tract and oesophagus which were treated with pentamidine given intramuscularly in a dose of 200 mg. every 12 hours for up to 14 days are reported from the University of Aarhus, Denmark. The leukaemic patient, who had signs of pneumonia and only *Candida albicans* in the sputum, responded rapidly and cultures of throat swabs were negative 6 days after cessation of treatment. Of the 2 patients with Hodgkin's disease one showed marked improvement, but *C. albicans* was still present in the oesophagus after 12 days; the other patient was infected with *C. albicans*, *C. pseudotropicalis*, and *C. krusei*; studies *in vitro* showed that growth of all three species was inhibited by a concentration of 0·002 mg. of pentamidine per ml. In this case initial improvement was noted but the infection had not cleared before the patient died suddenly 13 days after the beginning of treatment.

The authors suggest that the diamidines may prove useful in the treatment of moniliasis [but do not state whether the injections caused local or general reactions, as reported by Wolff *et al.* (*Lancet*, 1955, **1**, 991; *Abstracts of World Medicine*, 1955, **18**, 421)]. *R. F. Jennison*

44. Liver Biopsy in Sarcoidosis

G. MATHER, J. DAWSON, and C. HOYLE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 331–350, Oct., 1955. 9 figs., bibliography.

At King's College and Brompton Hospitals, London, the value of aspiration liver biopsy in the diagnosis of sarcoidosis was confirmed by the finding of epithelioid-cell follicles in specimens from 59 out of 93 patients who, on clinical and radiological grounds, were considered to be suffering from this disease. The incidence of hepatic follicles could not be correlated with the degree of tuberculin sensitivity or with hyperglobulinaemia. In 31 cases the effect of treatment with streptomycin and cortisone was studied in serial liver biopsies. Streptomycin did not appear to have any appreciable effect, whereas after administration of cortisone the follicles often regressed or disappeared. Liver biopsy was also carried out on 32 patients with various forms of tuberculosis; granulomata, indistinguishable from those found in sarcoidosis, were observed in 8.

[The identical histological findings in sarcoidosis and tuberculosis limit the value of this method in the differentiation of the two diseases. Deductions concerning the effects of treatment which are based on changes in minute miliary granulomata obtained by serial needle biopsies may not be valid, for the sampling error is great.]

D. Geraint James

Tuberculosis

45. **Antituberculous Immunity Induced by Methanol Extracts of Tubercle Bacilli: Its Enhancement by Adjuvants**

D. W. Weiss and R. J. Dubos. *Journal of Experimental Medicine* [*J. exp. Med.*] **103**, 73–85, Jan. 1, 1956. 14 refs.

It is possible to prepare from tubercle bacilli a fraction soluble in methanol which is capable of eliciting in mice a marked degree of resistance against virulent tuberculous infection. The immunity was evident whether the infective dose was large and caused a disease with a rapid course, or was very small and caused a disease of many months duration.

Active material has been obtained by extraction with methanol at 55° C. of bacterial cells killed with 2% phenol, and washed with acetone. The methanol extracts used in the present study have been prepared from the phenol-killed cells of a culture of B.C.G., and of the avirulent culture H37Ra. Vaccination of mice has been carried out by the intraperitoneal route, and the challenge infection (with a highly virulent bovine culture) by the intravenous route. Weight for weight, the protective activity of the methanol extract is smaller than that of the bacterial cells from which it is extracted, but its primary toxicity for mice is also considerably lower. The protective activity can be increased, and the immunity prolonged, by using certain adjuvants as vehicle for injection of the vaccine. An oil adjuvant mixture, and small amounts of a highly purified preparation of the somatic antigen of typhoid bacilli, have been found capable of enhancing and prolonging the antituberculous immunity induced by the methanol extract. Under appropriate conditions the resistance resulting from intraperitoneal injection of the methanol extract is of the same order as that which follows vaccination with whole killed tubercle bacilli or with living B.C.G.—[Authors' summary.]

46. **Tuberculosis of the Breast. A Review with the Additional Presentation of Ten Cases**

G. Schaefer. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 810–824, Dec., 1955. 2 figs., 19 refs.

The occurrence of tuberculosis of the breast in a pregnant woman led the author to review the incidence of this condition and its association with pregnancy. Among 743 pregnant patients with tuberculosis who were delivered between 1932 and 1954 there was no case of tuberculosis of the breast, although during the same period 10 cases occurred in non-pregnant patients. In 2,141 operations on the female breast performed in the past 5 years, 2 patients were found to have tuberculosis. The incidence reported from other hospitals ranges from about the same level up to 1·4%. The condition is not usually associated with advanced pulmonary tuberculosis. In the author's opinion primary tuberculosis of the breast is extremely rare, the most usual route of infection being retrograde lymphatic extension from the axillary nodes, the upper and outer quadrant being most often involved. The view that the infection is rarely haematogenous is supported by the rarity of bilateral lesions. Parity and lactation are probably of little importance as predisposing factors, but tuberculosis of the breast may in rare cases follow trauma or mastitis.

In the author's series of 10 cases the youngest patient was aged 20 and the oldest 72, the average age being 45·2 years; 7 were married and 4 had borne children. The general health of 5 of the patients was good; 2 gave a family history of tuberculosis and only one was aware of a past history of tuberculosis. In no case was there a history of lactation immediately preceding the onset of symptoms. Pathologically, nodular, sclerosing, and atypical forms are described. The sclerosing type may be mistaken for carcinoma. A painless lump is the commonest initial finding, followed usually by enlargement of the axillary lymph nodes. The untreated disease progresses to abscess formation. While radiography may occasionally be helpful, biopsy and bacteriological examination are the only reliable means of diagnosis. Treatment should consist in local excision of all tuberculous tissue, including the axillary lymph nodes, with pre- and post-operative antibiotic therapy.

Norman F. Smith

47. **Tuberculous Meningitis in Children Treated with Isoniazid, Streptomycin, and PAS**

R. Maggi, C. J. García Díaz, and F. C. Pfister. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 21–32, Jan., 1956. 3 figs., 30 refs.

The authors describe the treatment of 20 children aged one to 3 years suffering from tuberculous meningitis who were admitted to the Children's Hospital, Buenos Aires, between April, 1952, and April, 1954, and followed up to March, 1955. [A number of other cases had to be excluded for various reasons.] Treatment consisted in administration of isoniazid orally and streptomycin intramuscularly, with or without PAS intravenously, all in high doses for the first 3 months and in decreased doses for the next 3 or 4 months, until recovery; only 9 of the children were given streptomycin intrathecally. The authors state that " there was no special selection of the cases " for the two treatment groups.

The clinical response to treatment was similar in the survivors in both groups. Four of the patients died, of whom one had not had streptomycin intrathecally and 3 had; all these 4 patients were in deep coma on admission. Tubercle bacilli were recovered from the cerebrospinal fluid of all 9 children treated with intrathecal streptomycin, but from only 6 out of the 11 not so treated. None of the patients in whom no tubercle bacilli were found in the spinal fluid died.

Tentorial blocks were demonstrated by pneumoencephalography in 5 of the 9 treated intrathecally and in 4 of the 11 not given this treatment. Sequelae noted among the 16 survivors at follow-up consisted of mental retardation in 4 cases, and paraplegia, optic atrophy, and deafness in one case each; only 8 of the patients had no sequelae. The authors now see no advantage in giving intrathecal treatment and have abandoned its use.

[These results are poor compared with modern British standards, but most of the cases described appear to have been diagnosed in a much later stage than is now customary in Great Britain. Deaths occurring in patients who are moribund on admission are unavoidable by any form of treatment.] *John Lorber*

PULMONARY TUBERCULOSIS

48. **Selective Angiopneumography and a Correlative Study of Bronchography and the Histopathologic Findings in Tuberculous Fibrothorax**
R. CICERO, H. DEL CASTILLO, M. FERNÁNDEZ, and M. MOULÚN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 73, 61–71, Jan., 1956. 8 figs., 27 refs.

This communication from the General Hospital (National University of Mexico), Mexico City, is based on a study of 36 patients aged between 13 and 48 years who were suffering from tuberculous fibrothorax. On the ordinary postero-anterior film they all showed a hemithoracic opacity, with displacement of the mediastinal structures to the affected side. There was no oxygen consumption on the affected side and in all cases tubercle bacilli were present in the sputum.

Angiopneumography was performed in two phases. (1) A catheter was passed into the external jugular vein and 15 to 20 ml. of 70% diodone injected for the "global" angiogram. (2) In 32 cases the affected pulmonary artery was successfully catheterized and 8 to 12 ml. of the contrast medium injected for the selective angiogram. The main findings on the latter were dilatation of the main pulmonary artery, with marked diminution and narrowing of the branches; occasionally the branches were absent on the selective angiogram, and in no case were they revealed on the global angiogram. Bronchography was performed by direct catheterization, using 40% "lipiodol". The findings varied considerably, but usually there was bronchiectasis with stunted bronchi, and cavities were also often present.

Of the 36 patients, 19 were subjected to pneumonectomy. All the resected specimens showed diminution in size and were of fibrous consistency, several containing irregular cavities draining through ectatic bronchi. In some cases the lung was virtually a block of massive fibrosis in which bronchial and arterial arborization was almost entirely absent. In general, marked inflammatory and granulomatous infiltration and focal areas of caseous necrosis were seen. The most constant findings on microscopy of the arterial vessels were proliferation of the intima and hypertrophy of the muscular layer. The bronchi showed dilatation, and diminution or absence of muscular fibres; in some cases infiltration and destruction of cartilage were observed. No correlation was considered possible between the angiographic and the bronchographic findings.

Sydney J. Hinds

49. **Bronchography in Pulmonary Tuberculosis.** (A propos de la bronchographie lipiodolée dans la tuberculose pulmonaire)
R. ISRAËL, P. HERTZOG, J. GILBERT, D. UZZAN, and C. PERSONNE. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] 19, 785–800, 1955. 11 figs.

The authors, writing from the Hôpital Foch, Paris, review the bronchoscopic findings in 1,500 patients with pulmonary tuberculosis. As contrast medium they use "lipiodol" thickened with talc or sulphanilamide, and particular attention is paid to the posture of the patient during bronchography. They stress the advantage of using sufficient medium and of late exposures, films sometimes being taken after half an hour in order to confirm that affected bronchi did not fill, or when they wished to study the small or peripheral bronchi. All examinations were performed during the course of chemotherapy and in a quiescent stage of the disease; there were no untoward complications of the procedure.

The changes observed are classified in four groups as follows: (1) alterations in the bronchi throughout an entire lobe or segment, ranging from mere irregularities of the wall to gross dilatation, with crowding of all branches; (2) changes limited to stenosis or dilatation of one or two of the small bronchi, usually in relation to isolated cavities or solid foci; (3) persistent blockage of a single or of several bronchi, giving the appearance of a "false amputation", very different from the tapering, radish-root-like appearance seen in stenosis (Type 2); although these appearances may be misleading unless bronchography has been performed with the greatest care, they may be useful in helping to locate a lesion; (4) lastly, the change typical of the obviously diseased bronchus draining a collapsed segment or lobe. The authors point out that some of the more subtle changes seen in bronchograms often cannot be found in resected specimens of lung, but attribute this to the distortion and obliteration caused by the formalin in which the specimens are preserved. [The abstracter's own experience certainly confirms this.] *Arnold Pines*

50. **Bronchography in Pulmonary Tuberculosis**
P. FORGACS. *Thorax* [*Thorax*] 10, 309–313, Dec., 1955. 3 figs., 24 refs.

An attempt was made at Kettlewell Hospital, Swanley, Kent, to assess the value of bronchography in 120 cases of pulmonary tuberculosis. In one group of cases bronchial changes were expected because of lobar or segmental consolidation, rapid inflation of a cavity, or the presence of a large primary complex; in another group bronchography was performed before resection in order to determine the extent of the disease or accurately to locate a small lesion; while in a third group bronchograms were obtained for the purpose of excluding

bronchial stenosis in patients about to undergo collapse therapy. Bronchograms were also taken occasionally before and during pneumoperitoneum to study the degree of relaxation of individual segments. It is pointed out that bronchography has certain limitations—for example, stenosis and obstruction of peripheral bronchi are difficult to demonstrate. Cavities can rarely be outlined (2 cases only in the present series); and abnormal appearances regularly demonstrable are confined to variations in calibre and to deviation of the larger bronchi.

In 50 cases the bronchograms were normal, although in many of these the lungs still contained extensive and conspicuous lesions. Bronchial dilatation was observed in 33 cases, in 25 of which it was slight. Gross bronchial dilatation was not seen, even in segments or lobes destroyed by tuberculosis. Small diverticula projecting 1 to 2 mm. beyond the bronchial silhouette were noted in 16 cases, being commonly found on the inferior profile of the left upper-lobe bronchus and the main trunk of the lingula. The author states that these represent dilated ducts of the bronchial mucous glands. Stenosis of a segmental or lobar bronchus was demonstrated in 2 cases only and stenosis of a bronchus draining a cavity in 3. No complications occurred in this series of cases and spread of tuberculosis was not observed.

It is concluded that bronchography is of limited practical value and the information it provides, although useful, can often be obtained by simpler procedures. For locating lesions bronchograms are equal but not superior to lateral tomograms.

John H. L. Conway-Hughes

51. Indefinitely Prolonged Chemotherapy for Tuberculosis. An Appeal

A. S. Dooneief, K. E. Hite, and R. G. Bloch. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **96**, 470–477, Oct., 1955. 3 figs., bibliography.

Before the introduction of chemotherapy the incidence of relapse in pulmonary tuberculosis ranged from 24 to 56%. Short-term chemotherapy may also be followed by a relapse; a review of the patients discharged from the Montefiore Hospital, Westchester Division, New York, in the year 1951 because the disease was "arrested" showed that 15% had relapsed by 1955. Disease may become evident in other parts of the lung or bronchial tree after surgical excision of all visible lesions. It is emphasized that there are no reliable criteria of inactivity of residual lesions, and that it is impossible to predict which patients will remain well after treatment ceases. For these reasons and because there are combinations of drugs which effectively postpone the emergence of bacterial resistance over long periods, the present authors decided to try prolonged chemotherapy in a group of 172 patients after discharge from hospital. The ages of the patients ranged from 14 to 77 years. Of the total, 161 had active pulmonary tuberculosis (30 minimal, 111 moderately advanced, and 20 far-advanced), and 11 had active extrapulmonary tuberculosis; 53 were treated for 12 to 23 months, 96 for 24 to 35 months, and 23 without interruption for more than 3 years. All the patients received combinations of streptomycin, *p*-aminosalicylic acid, and isoniazid. Pulmonary resection was performed in 31 cases. There was relapse or exacerbation of tuberculosis in only 3 of the patients, a relapse rate of 1·7%. Drug toxicity was not sufficiently severe to call for cessation of treatment.

The authors conclude that since the optimum duration of drug treatment is not known, chemotherapy under close observation should be prolonged indefinitely.

Kenneth M. A. Perry

52. On the Prognosis of Childhood Tuberculosis. An Eighteen-year Follow-up Report

N. Levin. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 513–526, Oct., 1955. 1 fig., 20 refs.

The prognosis in primary and post-primary tuberculosis in childhood was studied at Länssanatoriet, Uttran, Sweden, from the follow-up findings in 434 patients who in 1935, when under 5 years of age and receiving sanatorium treatment for tuberculosis, were the subjects of an initial investigation in which repeated radiographs were taken and material obtained at gastric lavage was examined for the presence of *Mycobacterium tuberculosis* (*Acta paediat.* (*Uppsala*), 1935, **17**, Supp. 1, 160).

Signs of healed tuberculosis in the form of calcification or presumed fibrotic areas were observed at the follow-up examination in 33% of the cases in which the bacteriological findings on gastric lavage had been negative and in 43% of those in which the initial findings had been positive. Of special interest were the follow-up observations in cases of active tuberculosis of the lungs or hilar lymph nodes, a comparison being made between the findings in cases of primary pulmonary tuberculosis at the initial examination and those in cases of post-primary disease. There was a marked difference between the mortality rate in children with primary lesions (7%) and the rate in those with post-primary disease (63%). Mortality in the former group increased according to the age at which the disease was detected. In children under 10 years at the time of diagnosis the mortality ranged from 3 to 6%, while in children aged 11 to 15 years it was 18%. This, the author states, reflects the heightened risk of tuberculosis during puberty. In children who initially had post-primary tuberculosis the death rate in all age groups was considerably higher than in those with primary tuberculosis.

Of the children in whom there were primary lesions initially and tubercle bacilli were recovered from gastric lavage material, 88% showed no signs of active disease at the time of follow-up, and 4% had active lesions; the corresponding figures for primary tuberculosis with negative bacteriological findings were 92% and 4%. This, it is suggested, indicates that the results of bacteriological tests of gastric lavage material during the acute phase of the disease lack prognostic significance.

Altogether 34 of the original patients had died; 8, including 5 with primary tuberculosis, died from tuberculous meningitis, most of them in early childhood.

John Taubman

Venereal Diseases

53. Venereal Disease in Prostitutes Treated at the Hospital do Desterro, Lisbon. (Venereologia nas meretrizes assistidas no Hospital do Desterro)
M. SAMPAIO and M. CHAVES. *Trabalhos da Sociedade portuguesa de dermatologia e venereologia* [*Trab. Soc. port. Derm. Vener.*] **13**, 255–266, Dec., 1955.

During the 10 years ending October, 1955, 3,866 prostitutes were admitted to the Hospital do Desterro, Lisbon, the annual admission rate varying between 310 and 459. Until 1948 the number of registered prostitutes admitted outnumbered that of the *clandestinas*. After 1949 there was a marked fall in the number of registered prostitutes as a result of a law passed that year forbidding fresh registrations or the opening of new brothels; at the same time there was a big increase in the number of clandestine prostitutes admitted. The authors detail the venereal infections found in 235 prostitutes during the year ending October, 1955, the routine tests carried out on each patient including serological tests for syphilis, smears and cultures for gonorrhoea, and vaginal smears for *Trichomonas vaginalis* and *Monilia*. Early syphilis was found in 13 cases (5·5%), latent syphilis in 60 (25·5%), " gonococcal vulvovaginitis " in 82 (34·8%), trichomonal vaginitis in 93 (39·5%), monilial vaginitis in 13 (5·5%), soft sore in 5 (2·1%), and genital warts in 28 (11·9%); 49 prostitutes had two or more of these conditions. Frei and Ito tests were carried out on 163 women, the latter giving a positive result in 55 cases (33·7%) and the former in 14 (8·5%). The social problems are discussed. It is noted that 70 of the women were married and 9 were pregnant, while of 167 women questioned, 110 were illiterate. *Eric Dunlop*

54. Serological Findings in Leprosy and Tuberculosis with the Wassermann, Meinicke, and VDRL Tests
H. RUGE. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **13**, 861–886, 1955. 35 refs.

During a venereal disease survey carried out by the World Health Organization in Egypt, sera from 820 lepers and 720 patients with tuberculosis were subjected to the Kolmer Wassermann reaction using cardiolipin antigen (W.R.), the Meinicke test, and the V.D.R.L. slide test. The incidence of syphilis in the general population was found to be 2 to 4%, and it was estimated that between 2 and 4% of all positive or doubtful reactions were probably non-specific in nature.

Among the 820 sera from cases of leprosy, mostly from inmates of a leper colony and some from patients attending out-patient clinics, there were 234 positive reactions; 16 of these patients had a history of syphilis and a further 15 were considered to be syphilitic on the grounds that positive reactions were obtained with all or most of the tests used. [This assumption may be open to question.] In 25% of cases the reactions were thought to be non-specific. These were commonest in the cutaneous and mixed forms of the disease (25 to 50%) and least frequent in neural leprosy (10%). The Meinicke test was the most specific of those used and the V.D.R.L. test the least specific, while the W.R. occupied an intermediate position. Of 521 sera from lepers whose clinical histories were known, 5·4% of the reactions were anticomplementary, these being more common in males than females. In contrast only 0·9% of 25,000 sera examined during the general survey gave anticomplementary results.

Sera were tested from 592 patients with pulmonary tuberculosis and from 128 with tuberculosis of bone. There were 75 positive reactions; 8 of these patients had a history of syphilis, while a further 29 were considered to be syphilitic on serological grounds. Thus 5% of the whole group were thought to give non-specific reactions. In contrast to the findings in leprosy, the V.D.R.L. test had the highest specificity, followed by the Meinicke test and the W.R.

Discrepancies were fewer and less marked between the results of the three tests on the sera from the tuberculous patients than on those from lepers, the pattern of the reactions being more uniform. Quantitative V.D.R.L. tests were performed on all sera reactive to the slide test. With one exception sera giving titres greater than 1:4 also gave positive Wassermann and Meinicke reactions. [The serological results are analysed in great detail; they do not lend themselves to presentation in abstract form.] *A. E. Wilkinson*

55. A New Complement-fixation Technique in the Serology of Syphilis. (Nouvelle technique de fixation du complément dans la sérologie de la syphilis)
G. M. P. ROULIN. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **13**, 887–902, 1955. 9 refs.

The author describes a complement-fixation technique for the diagnosis of syphilis, developed at the Lille Military Hospital, which combines features of the Calmette–Massol and Kolmer methods. The complement dosage is kept fixed at 0·2 and 0·3 ml. of a 1:40 dilution of guinea-pig serum, 0·1 ml. of the serum under test and 0·1 ml. of diluted cardiolipin antigen completing the test mixture. Incubation is for 22 to 23 hours at 6 to 8° C., followed by 30 to 35 minutes at 37° C. Haemolysin is titrated in the presence of 0·2 ml. of 1:40 complement, and a 5% cell suspension sensitized with 3·5 M.H.D. of haemolysin is used in the test. [Very full details of the technique are given in the original paper.] By cutting down the amount of complement the author claims to have considerably raised the sensitivity of the test.

In tests carried out in parallel with the Meinicke, Kahn, Kolmer, and V.D.R.L. tube tests on 1,700 sera sent for routine examination the author's technique gave isolated positive reactions in 19 instances. These included 6

cases of known and 6 of possible syphilis, 4 cases in which no clinical history was available, and 3 cases in which there was no evidence pointing to syphilis. [The author's assumption that a positive reaction was specific if any one (or more) of the other reactions was also positive is perhaps open to question.]

Sensitivity was assessed by tests on syphilitic sera in parallel with the Meinicke, standard Kahn, V.D.R.L. tube, and Kolmer tests, in which the same antigen was used as in the author's test. With the exception of the Meinicke, the author's test was considerably more sensitive than the others. In a series of quantitative tests it gave higher titres than either the V.D.R.L. tube test or the Kolmer test with cardiolipin. *A. E. Wilkinson*

56. Value of the Kahn Test in Africans

A. J. EVANS. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 210–227, Dec., 1955. 1 fig., bibliography.

After a lengthy review of the literature concerning the cause, nature, and incidence of biologically false positive reactions in serological tests for syphilis, the author presents the results obtained with the Kahn test performed on 6,006 adult African patients attending venereal disease clinics in Northern Rhodesia. In 1,889 of these the test was persistently positive although no clinical manifestations of active syphilis could be found. It was estimated, after clinical assessment of each patient, that in 9 to 17·5% of these "potential" latent syphilitics the reaction was falsely positive—that is, an incidence of 2·8 to 5·5% of the total number studied.

In addition to the above, the Kahn test was carried out on 137 patients known to have malarial parasites in the blood [presumably with no signs suggestive of syphilis]. Of these, 38 (27·7%) were found to give a positive or weakly positive result. A higher incidence of positive results occurred among children suffering from malaria than among adults. In a study of 447 patients with leprosy a positive or weakly positive result was obtained in 18·4%. Positive reactions were twice as common in female as in male lepers and they were also more frequent among the patients with lepromatous lesions than in those with other types of the disease. The author concludes that in Northern Rhodesia a positive Kahn reaction usually denotes syphilitic infection, and he [rightly] deprecates the practice of disregarding positive reactions in Africans because of the absence of clinical signs of the disease.

[This report of a careful study will be read with profit by all who are responsible for the care of patients in or from tropical countries.] *G. L. M. McElligott*

57. Prognosis of Cardiovascular Syphilis

A. GRIMBLE. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 239–253, 1955. 2 figs., 41 refs.

After a comprehensive review of the literature on cardiovascular syphilis, especially of reports concerning prognosis and the value of specific therapy, a study is presented of 164 cases (143 males and 21 females) seen at Guy's Hospital, London, between 1925 and 1944. Of the 164 patients, 92 were given organic arsenicals intravenously while 72 did not receive antisyphilitic treatment. None was given antibiotics.

The cause of death in almost all instances was cardiac or pulmonary disease; 12 patients died from ruptured aneurysm. Post-mortem examination was carried out in 36 of the 164 cases. In retrospect it was found extremely difficult to grade the size of the heart or the degree of cardiac failure, but it is of interest that pain in the chest occurred in just over one-half of the 145 patients in whom the duration of symptoms could be accurately ascertained. The average age of the patients in this series was 54 years (31 to 71), those with aneurysm in both treated and untreated groups being on the average 4 years older than those with valvular disease. The mean expectation of life was 2 to 4 years, with a maximum of 12 years; this is in close agreement with the findings of other workers. Treatment with organic arsenicals increased the expectation of life after the onset of symptoms from 32 to 51 months; this also is in line with the findings of others. The results of specific therapy were best "in the younger patients, more strikingly in those with valvular disorder, than those with aneurysm". *G. L. M. McElligott*

58. Skin Testing in 246 Patients with Non-specific Urethritis, with a Review of the Important Literature

A. GRIMBLE and G. W. CSONKA. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 228–234, Dec., 1955. Bibliography.

As a contribution to the controversial subject of the aetiology of non-specific urethritis the authors undertook, at various clinics in London, a study to determine whether an altered skin sensitivity could be shown to exist in the majority of cases of non-specific urethritis and, if so, whether this skin response was of a specific nature. The antigen for skin testing was prepared from the urethral secretions of patients suffering from non-specific urethritis, the urethral scraping being mixed with normal saline. This mixture was first centrifuged for 15 minutes and the supernatant fluid then withdrawn and incubated at 60° C. for one hour. The fluid was tested for bacteriological sterility before use and 0·5% phenol was added. Control of the donor skin-test material was effected by (*a*) using a control injection of 0·5% phenol in normal saline; (*b*) preparing an antigen in a similar manner from cases of acute gonorrhoea; and (*c*) skin-testing a group of patients who did not have non-specific urethritis. The test was considered positive when there was a papule with erythema 1 cm. or more in diameter.

Of 137 cases of non-specific urethritis, 53·3% gave a fully positive result and 30% a clearly negative result, while the remaining 16·7% gave weakly positive reactions. Only one out of 34 cases of acute gonorrhoea gave a positive result, as did also only one out of 36 patients with no sign or history of urethritis of any type. It is concluded that these findings suggest that between 50 and 70% of cases of urethritis are due to a predominating cause, and that it is likely that this is an infective agent.

[There is a useful review of the literature, over 80 references being cited.] *G. L. M. McElligott*

Tropical Medicine

59. Dieldrin in Granulated Form as a Mosquito Larvicide. I. Results of Trials Carried out in Artificial Earth Pools. II. Results of Trials Carried out in Natural Pools

G. WEBBE. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **49**, 353–355 and 356–361, Dec., 1955. 4 refs.

Insecticides in oily form are unsuitable for use in mosquito control in swamps and ponds containing much vegetation and in such circumstances a granulated insecticide is preferable to a dust. To study the efficacy of granulated "dieldrin" for this purpose, artificial pools of water, 9 inches (22·8 cm.) deep and with a surface area of 5½ square yards (4·6 sq. m.) were made in concrete boxes lined with soil. A known number of *Anopheles gambiae* 4th-stage larvae were put into the water, and a calculated quantity of 1% dieldrin granules scattered on the surface. All the water was baled out 48 hours later and the surviving larvae collected and counted. The minimum lethal dosage was found to be 5 oz. per acre (353 g. per hectare). The presence of vegetation had no apparent effect upon the activity of the larvicide.

Six natural ponds in the coastal region of Tanganyika, with surface areas of 0·3 to 18·5 acres (0·12 to 7·48 hectares) and with varying proportions of vegetation and open water were then treated on 8 successive weeks in the dry season with 10 oz. per acre (706 g. per hectare) of 1% dieldrin granules, which were scattered from the bank by hand. After the second application all anopheline and almost all culicine larvae had disappeared. Larvae in floating cages towed to the middle of one of the ponds after the second application died within 48 hours. Culicine larvae reappeared in the ponds 4 weeks and anopheline larvae 6 weeks after the last application. That the larvicide was not so effective in natural ponds as in artificial pools was probably due to the greater depth of water in the former. May-fly, dragon-fly and damsel-fly nymphs, bugs, water-boatmen, and beetles disappeared from the ponds after the third application of dieldrin. Frogs and crabs were unaffected. *L. G. Goodwin*

60. Comparison of Milk and Soya Beans in the Treatment of Kwashiorkor in Uganda

M. D. THOMPSON. *British Medical Journal* [*Brit. med. J.*] 2, 1366–1369, Dec. 3, 1955. 5 refs.

In a study carried out at Mulago Hospital (Makerere College), Kampala, Uganda, the author has compared the value of skimmed cow's milk with that of a soya-bean preparation in the treatment of kwashiorkor in 92 infants, all of whom had oedema or a low serum protein level, characteristic changes in the colour or texture of the hair, and skin lesions; patients whose condition was regarded as dangerous were all treated with milk. The milk treatment consisted of reconstituted skim-milk powder preceded by or reinforced by administration of calcium caseinate, a concentrated milk protein. Later in the study the amount of milk was restricted so as to provide from 2·5 to 3 g. of protein per kg. body weight per day in order to allow comparison with the soya-fed group. The soya beans were prepared by the method described by Dean (*Brit. med. J.*, 1952, **2**, 791; *Abstracts of World Medicine*, 1953, **13**, 201). Vitamins (including vitamin B_{12}) and methionine were given to some children. The criteria of clinical progress were loss of anorexia, loss of pitting oedema, increase in body weight, healing of skin lesions, and improvement of temperament. It was found that sufficient milk to ensure at least 2·5 to 3 g. of protein per kg. body weight per day was necessary in order to initiate recovery. No real difficulty was encountered in feeding, but use of a nasal tube was occasionally required.

Of the 35 children given the milk diet, good progress occurred in 22, although diarrhoea was troublesome, while of the 42 given the soya preparation, good progress was noted in 14 only; in 15 cases the diet had to be changed from soya to milk owing to lack of improvement and in 8 of these progress was then good. The addition of vitamins or methionine to the diet did not result in a better response to soya. The author concludes, therefore, that milk products should be used in the treatment of kwashiorkor, but that soya protein may be of use in preventing its development.

W. H. Horner Andrews

INFECTIOUS DISEASES

61. Isoniazid in Leprosy

R. F. R. SCRAGG. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **49**, 548–554, Nov., 1955. 11 refs.

The results obtained with isoniazid in the treatment of leprosy have not hitherto been favourable. In 6 adult lepers at the Anelaua Hansenide Colony, New Ireland, the author tried a higher dosage than that employed in previous investigations—namely, 4 mg. of isoniazid per kg. body weight daily for the first 5 weeks, increased thereafter to 8 mg. per kg. daily. The patients, 4 males and 2 females, had been treated with "sulphetrone" (solapsone) unsuccessfully. The period of observation was approximately 11 months to 2 years.

There was some symptomatic improvement in 4 cases and bacteriological improvement, as shown by a reduction in the bacillary content of the lesions with fragmentation of bacilli, in all the cases. Lepra reactions occurred in one patient at the start of treatment and in another during administration of isoniazid; the course of these reactions did not appear to be influenced by the drug. Neuritis, which developed in 2 cases, was attributed to isoniazid therapy; no other toxic reaction

was noted. The author considers that isoniazid has a definite place in the treatment of leprosy, and is an effective alternative to the sulphone group of drugs.

William Hughes

62. Chloramphenicol and Penicillin in the Treatment of Leptospirosis among British Troops in Malaya

A. C. FAIRBURN and S. J. G. SEMPLE. *Lancet* [*Lancet*] **1**, 13–16, Jan. 7, 1956. 1 fig., 34 refs.

Conflicting reports have been published on the value of antibiotics in the treatment of leptospirosis; in view of this and of the prevalence of the condition among British troops in Malaya, the authors carried out a controlled trial of penicillin and chloramphenicol on 83 patients, aged 18 to 35 years, 71 of whom were British. The patients were divided into three groups—Group 1 (31 patients) served as controls; Group 2 (21 patients) received penicillin; and Group 3 (31 patients) received chloramphenicol. The dosage of penicillin was 600,000 units 6-hourly and that of chloramphenicol 0·5 g. 6-hourly, administration being continued until the patient had been free from symptoms and signs for 24 hours, which, in most cases, was at least 5 days.

No significant difference was observed between the three groups, either in the time required for the patient to become symptom-free or in the incidence of complications. The authors conclude that these 2 antibiotics are unlikely to be of value in the treatment of this disease.

W. K. Dunscombe

63. Suppression of Malaria by Monthly Drug Administration

M. J. MILLER. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 790–799, Sept., 1955. 3 figs., 3 refs.

At the American Foundation for Tropical Medicine, Harbel, Liberia, the author studied the effect of pyrimethamine and chloroquine given separately and together at monthly intervals and of primaquine given weekly on 217 West African school children aged 5 to 14 years. Malaria is hyperendemic in this area and *Plasmodium falciparum* is the predominant species. The children attended schools in three different areas and groups were treated as follows: Group 1, 60 children, one 25-mg. tablet of pyrimethamine monthly for 8 months; Group 2, 33 children, one 15-mg. tablet of primaquine weekly for 12 weeks; Group 3, 32 children, one 0·15-g. tablet of chloroquine (base) monthly for 8 months; and Group 4, 42 children, one tablet of pyrimethamine and one of chloroquine at monthly intervals for 6 months. A control group in each area (total number of controls, 50) received a placebo or were not treated at all. The malaria parasite rate, the spleen rate, and the average enlargement of the spleen were determined before treatment started and again each time a drug was given.

Pyrimethamine once a month effectively suppressed malaria in these semi-immune children; it afforded better protection and had a more prolonged suppressive effect than chloroquine. When these two drugs were given together the results were no better than when pyrimethamine was given alone. Primaquine once a week had little effect on the malaria asexual parasite rate. There was an apparent inhibition of gametocyte production in the blood in children given these drugs, but there was no evidence that the spleen rate or the average enlargement of the spleen was influenced by treatment. Contrary to the findings of Clyde and Shute (*Trans. roy. Soc. trop. Med. Hyg.*, 1954, **48**, 495; *Abstracts of World Medicine*, 1955, **17**, 451) the development of pyrimethamine-resistant strains of plasmodia was not observed. The results suggest that a single dose of pyrimethamine will suppress malaria parasitaemia for periods up to one month.

A. G. Shaper

64. Amebic Hepatitis. Laboratory Findings and Treatment with Erythromycin

T. L. NELSON, H. H. ANDERSON, and O. THOMAS. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 812–821, Sept., 1955. 4 figs., 14 refs.

During the year 1954 a total of 371 cases of intestinal amoebiasis were seen at the Sonoma State Hospital, Eldridge, California, in 29 of which there was evidence of abnormal liver function. In order of usefulness the diagnostic procedures employed were the cephalin flocculation test, liver biopsy, estimation of the urinary excretion of urobilinogen and of the erythrocyte sedimentation rate, palpation of the liver, and *x*-ray examination of the chest for pulmonary involvement in the right lower lobe and of the abdomen for liver size. Fever, leucocytosis, and an abnormal response to the "bromsulphalein" retention test were frequently observed. The pulmonary involvement ranged from increased bronchovascular markings to pulmonary infiltration. [No control group is mentioned.] In 9 of the 11 patients subjected to liver biopsy a subacute hepatitis was manifested by increased lymphocyte and plasma-cell infiltration in the periportal areas.

Of the 29 patients, 28 received erythromycin stearate for 14 days in a daily dosage of 1 g. for adults and 15 mg. per kg. body weight for children; one patient with severe diarrhoea received erythromycin and fumagillin together for 14 days. In 20 patients the liver condition responded favourably, the results being considered "good" in 18 and "fair" in 2. In the remaining 9 patients the response was unsatisfactory, but in 6 of these subsequent treatment with chloroquine proved effective.

A. G. Shaper

65. Erythromycin in Amebiasis

G. MCHARDY, D. C. BROWNE, R. J. MCHARDY, and S. S. WARD. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 998–1001, Nov., 1955. 6 refs.

The authors have studied, at Louisiana State University School of Medicine, New Orleans, the amoebicidal activity of erythromycin stearate in 42 cases of amoebiasis, all of which were free of extra-intestinal involvement. The drug was given in film-sealed tablets in a dosage of 800 mg. per day in 4 equal doses for 10 days (total dose 8 g.), faecal examinations being carried out at intervals for 6 months after completion of treatment; of these patients, 5 relapsed, one after 30 days, 3 after 60 days,

and one after 6 months. A further small group of 8 cases received 800 mg. of a suspension of erythromycin stearate per day for 10 days; *Entamoeba histolytica* persisted in 2 patients at the end of treatment, while a third patient relapsed 30 days after treatment.

Considering the two series together the drug eliminated *E. histolytica* in 42 cases (84%) out of 50 treated. Side-effects such as nausea, abdominal cramping, mild diarrhoea, and pruritus ani occurred in only 6 (12%) of the patients and were limited to the period of treatment. The authors conclude that erythromycin, when given alone, is less effective than oxytetracycline or fumagillin. However, it is more effective if used in combination with "mantomide". *R. A. Neal*

66. Fumagillin and Erythromycin in the Treatment of Amebiasis

R. C. JUNG, A. GARCIA-LAVERDE, and F. F. KATZ. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 989–997, Nov., 1955. 20 refs.

The results of preliminary studies of the use of fumagillin and erythromycin stearate in the treatment of amoebiasis are reported from Tulane Medical School, New Orleans. Fumagillin was given in capsules in a dose of 10 mg. three times per day for 7 days (total dose 210 mg.). Faecal examinations 6 weeks after completion of treatment showed that 10 out of 14 cases had been cleared of *Entamoeba histolytica*, 9 out of 11 cases of *Entamoeba coli*, but none of 8 cases infected with *Endolimax nana*. Erythromycin was given to 8 adults in doses of 600 mg. every 6 hours for 7 days (total 16·8 g.). The patients all developed mild diarrhoea, but all signs of infection due to *E. histolytica* alone (3 cases) and to this organism and *E. coli* (5 cases) were eliminated. Another group of 16 adults and children were then given a lower dose of erythromycin, namely, 30 mg. per kg. body weight up to 1,600 mg. per day in 2 to 4 doses for 7 days. At the end of treatment one patient still showed *E. histolytica* in the stools and a further 4 relapsed within 40 days. Dysenteric symptoms which occurred in 4 cases were relieved within 2 days of the beginning of treatment, but in one case amoebae reappeared and dysentery recurred after 2 weeks. No side-effects due to the drug were observed.

A clinical trial of these drugs on a larger scale was then carried out in Darien Province, Panama, mainly among school-children. Stools were examined by direct smear and also after concentration by the zinc sulphate technique, many of the specimens being examined within one hour. Among 752 subjects, 21% were infected with *E. histolytica*, while the incidence of the non-pathogenic amoebae was much greater, being 49·7% for *E. nana* and 59% for *E. coli*. Children infected with *E. histolytica* were treated for 7 days with sugar-coated tablets containing 10 mg. of fumagillin or 100 mg. of erythromycin stearate, or a combination of the two drugs in a dosage varying from 10 to 30 mg. per day for fumagillin and 200 to 1,200 mg. per day for erythromycin according to age of the patient. At the end of the course of treatment all species of amoebae had disappeared from the stools, though the non-pathogenic amoebae reappeared in 27 to 44% of patients and *E. histolytica* reappeared in about 6%. Of cases of infection with *E. histolytica*, fumagillin alone cleared 33 out of 39 (85·3%), erythromycin alone cleared 18 out of 18 (100%), while the two combinations of fumagillin (5 or 10 mg.) and erythromycin (100 or 150 mg.) cleared all of 31 cases (100%) and 31 out of 32 (96·9%) respectively. The drugs had no effect upon balantidiasis. Side-effects of the treatment were not troublesome.

The authors conclude that although fumagillin and erythromycin are useful amoebicidal drugs which can be employed when other drugs are contraindicated, neither should be used indiscriminately: for fumagillin has been observed to produce leucopenia, and as the most valuable property of erythromycin is its efficacy in the treatment of penicillin-resistant staphylococcal infections, routine use of the antibiotic in amoebiasis is likely to produce cocci which are resistant to both erythromycin and penicillin. *R. A. Neal*

67. Non-bancroftian Elephantiasis in Tanganyika

P. JORDAN, M. H. TRANT, and W. LAURIE. *British Medical Journal* [*Brit. med. J.*] **1**, 209–210, Jan. 28, 1956. 7 refs.

Examination of night blood samples from 475 adults in four villages in an area to the south-west of Lake Victoria, Tanganyika, about 4,000 to 5,000 feet (1,220 to 1,830 metres) above sea level did not reveal any evidence of infection with microfilariae of *Wuchereria bancrofti*. Moreover, it was known that onchocerciasis did not occur in this area. Nevertheless, 12 cases of elephantiasis of the legs were found, and on a subsequent occasion 62 further cases were detected [the total population sampled is not stated]. The disease was unilateral in 15 (20%) of these 74 cases, and in 29 (39%) there was inguinal lymphadenitis; the corresponding percentages in areas in which bancroftian infection was endemic were 55 and 60% respectively. Hydrocele also was less common in non-bancroftian elephantiasis. The incidence of the disease was highest in the age group 21 to 30 years. The authors discuss the possibility that these cases were due to infection with *Acanthocheilonema perstans*, the larvae of which were present in 145 out of the original 475 specimens of night blood. The adult worm lives in the peritoneal cavity of the host without causing tissue reaction, and in the authors' view it is not unreasonable to suggest that on occasion the adult may enter the abdominal lymph nodes and initiate tissue changes which cause blockage. No post-mortem evidence was available, but it is noted that microfilariae of *A. perstans* have frequently been found on puncture of enlarged femoral lymph nodes [though their presence in such a vascular organ is of doubtful significance].

[In view of the age at which the incidence of elephantiasis was highest and the high incidence of venereal disease in this area lymphogranuloma venereum should have been excluded as a possible cause of the condition, the clinical picture of which at its onset differed in several respects from that of bancroftian infection.]

Clement C. Chesterman

Allergy

68. **Past History and Skin Reactions in Allergic Children.** [In English]
F. JENSEN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] 9, 188–202, 1955. 4 figs., 6 refs.

At the University Hospital, Copenhagen, the skin reactions of 600 children with allergic diseases, mainly asthma, were investigated between 1948 and 1952, to determine their relation to allergic symptoms. From the past histories of these children it was found that house dust, feathers, moulds, and grass pollens were the most important inhalant allergens, and the greatest conformity between the past history of sensitivity and the skin reactions was found with house dust, 71% of those sensitive giving a positive skin reaction. It is stressed that in allergic children bacterial allergens occur as the sole releasing factor in 33% of cases.

A. W. Frankland

69. **Allergic Reactions in Sites Recurrently Infected with Hemolytic Streptococcus**
F. A. STEVENS. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 185–188, Feb., 1956. 10 refs.

70. **Topical Use of Prednisolone in Nasal Allergy. Report of a Controlled Study**
J. R. ANDERSON and H. D. OGDEN. *Annals of Allergy* [*Ann. Allergy*] **14**, 44–46, Jan.–Feb., 1956.

A solution containing either 0·5 mg. or 1 mg. of prednisolone per ml. was sprayed into the nostrils of patients with proved allergic rhinitis, 10 patients receiving each solution, while 10 others received a placebo. During the first 48 hours of treatment the total daily dose was probably less than 1 ml. of solution in each case, and thereafter it was reduced to about one-fifth of this quantity. The double-blind technique was used in the trial. None of the patients who received the placebo spray reported a definite improvement. The prednisolone sprays caused various degrees of subjective improvement in all patients and there was also a decreased amount of mucus secretion.

[The results would appear more convincing if more details were given about the degree of allergic rhinitis in the patients treated, in particular with regard to blockage of the airway, and also about objective improvement during and after the trial.] *H. Herxheimer*

71. **Toxicologic and Clinical Appraisal of Buclizine, a New Antihistaminic Compound**
I. W. SCHILLER and F. C. LOWELL. *Journal of Allergy* [*J. Allergy*] **27**, 63–67, Jan., 1956. 8 refs.

The authors report, from Boston University School of Medicine, the clinical trial of a new antihistaminic compound, "buclizine", (1-*p*-chlorbenzhydryl-4-*p*-tertiary butylbenzylpiperazine hydrochloride). They showed that in the guinea-pig this substance, in a dose of 1 mg. per kg. body weight, had the remarkable property of protecting these animals against the lethal effects of a histamine aerosol for up to 16 days. However, when given in doses of 25 to 75 mg. per day orally to 70 patients, most of whom were suffering from allergic rhinitis, the duration of action was only a few hours. It improved the condition in about two-thirds of the cases; the usual side-effects of antihistamines occurred in 18 cases (26%). It is suggested that the marked difference in duration of action in guinea-pigs and man requires further study.

H. Herxheimer

72. **Actinomycin C, Anaphylaxis, and Allergy.** (Actinomycine C, anaphylaxie et allergie)
L. BUSINCO. *Presse médicale* [*Presse méd.*] **63**, 1687–1688, Dec. 3, 1955. 7 refs.

Because of the effect of actinomycin C on lymphatic and reticulo-endothelial tissues, the author, working at the University of Rome, has investigated its influence on the formation of antibodies. The drug does not prevent fatal anaphylactic shock due to the injection of egg albumen in sensitized guinea-pigs, but favourable results are claimed in allergic conditions in man with a dose of 40 to 150 μg. given daily for 3 weeks. Bronchial asthma and chronic urticaria are considered particularly suitable for treatment. Electrophoretic examination of the plasma in treated patients shows a fall in the gamma globulin content. *P. C. Reynell*

73. **A Pharmacodynamic Test for the Assessment of Severity in Asthma. Estimation of the Excitability of the Lung by Acetylcholine.** (Évaluation du degré de l'asthme par une épreuve pharmacodynamique. La mesure de l'excitabilité acétylcholinique du poumon)
R. TIFFENEAU. *Annales de médecine* [*Ann. Méd.*] **56**, 582–602, 1955.

In a study carried out at the Hôtel-Dieu, Paris, of the sensitivity of the bronchial tract to acetylcholine as a measure of severity in asthma, an aerosol of acetylcholine was administered and the threshold doses which produced a lowering of the vital capacity at rest and after effort were observed. In normal subjects the administration of less than 10,000 μg. did not alter the vital capacity. In patients with "latent" asthma, that is, those who had never experienced an attack of asthma but had related manifestations such as eczema, or who had a family history of asthma, the lowering of the threshold of sensitivity to acetylcholine was not marked. In contradistinction, in patients with bronchial asthma this threshold was reduced markedly and more or less constantly, being diminished both during attacks and in remission; nor did the reduction run parallel with the degree of exposure to precipitating factors such as dust and fumes, or with the presence of bronchial infection. The sensitivity to acetylcholine was highest in patients

with chronic asthma, who often also had emphysema. The author claims that the acetylcholine sensitivity test distinguishes this last type of case from those of non-asthmatic emphysema, since in the latter no marked changes of tolerance to acetylcholine are found.

Kate Maunsell

74. Eosinophilic Pleural Effusions in Asthma. (Les épanchements pleuraux à cellules éosinophiles au cours de l'asthme)

J. TURIAF. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 4117–4123, Dec. 22, 1955. 1 ref.

In the last 10 years the author has seen 21 cases of eosinophilic pleural effusion (excluding those due to intestinal parasites) among patients with asthma at the Cochin and Bichat Hospitals, Paris. In some of these cases the effusion occurred in small quantity for 2 to 7 days after transitory infiltrations of the lung near its pleural surface (especially in the costophrenic angle), and was often accompanied by brief fever and general disturbance. The blood and marrow also showed an eosinophilia. The differentiation from Loeffler's syndrome and eosinophilia due to intestinal parasites was difficult.

In other cases the effusion occurred in asthmatic patients with spontaneous pneumothorax. Thus among 19 cases of pneumothorax, there were 6 cases of effusion, 5 of which were eosinophilic. In these again the effusion was small, but easy to recognize radiologically. It lasted 4 or 5 days, and was not accompanied by a blood eosinophilia. Treatment was unnecessary, and there were no complications.

G. C. R. Morris

75. Prognosis in Bronchial Asthma. A Study of the Mortality among Patients Discharged during the Years 1917–1936 from the Ullevål Hospital (Oslo City Hospital)

K. WESTLUND and A. HOUGEN. *Journal of Chronic Diseases* [*J. chron. Dis.*] **3**, 34–45, Jan., 1956. 3 refs.

In a study of the mortality from bronchial asthma 327 (94·8%) of the 345 patients discharged from the Ullevål Hospital, Oslo, between 1917 and 1936 with a diagnosis of asthma or asthmatic bronchitis have been followed up until death or until July 1, 1953. At this date 183 (82 males, 101 females) had died, the cause of death being certified as "asthma" in 41 cases (22%), "pneumonia and bronchitis" in 23 (12·5%), "cor pulmonale" in 2 (1·1%), and "myocardial disease" in 39 (21%).

Using life tables, the authors have compared the mortality among these asthmatic patients with that in a comparable group (standardized for age, sex, and year) derived from the general population of Oslo. The asthmatic patients had an excessive mortality at all ages. The actual number of deaths among male asthmatics was about twice the number expected on the basis of mortality in Oslo over the same period. The prognosis for females was worse, especially in the first 10 years after discharge from hospital, the mortality ratio being 2·5. There was no appreciable difference in mortality ratio between patients discharged during the period 1917–28 and those discharged between 1929 and 1936. The prognosis for patients who developed their first attack of asthma on the basis of chronic bronchitis or an upper respiratory infection was not significantly different from that for those with no history of respiratory symptoms. [This last finding must be accepted with reserve since in this series the number of patients who developed asthma without previous respiratory symptoms was very small.]

E. Keith Westlake

76. Vaccine Therapy in Bronchial Asthma. [In English]

G. BERGQUIST. *Acta allergologica* [*Acta allerg. (Kbh.)*] **9**, 97–106, 1955. 11 refs.

The results obtained with a polyvalent autogenous bacterial vaccine prepared from nasal (epipharynx) and throat swabs in the treatment of intrinsic asthma are reported. Different culture media were employed for the different bacteria, and in the preparation of the vaccine bacteria were used in the same proportions as they occurred in the swab. The initial dose of the vaccine contained 1,000,000 bacteria or less. All the patients, who were aged 41 to 50, were followed up for a minimum period of 12 months and the results compared with those obtained in a similar group of asthmatics given an autogenous vaccine prepared from *Staphylococcus aureus* and *Staph. albus*. With the latter vaccine the results were good in 76·4% of cases compared with 58% of the cases given the polyvalent vaccine. In a third (control) group receiving injections of vegetable protein the results were good in 15% of cases. It was also found that the results obtained with a polyvalent vaccine containing staphylococci were significantly better than those achieved with the polyvalent vaccine without staphylococci. A seasonal variation in the bacterial flora was noted.

A. W. Frankland

77. High and Low Dosage Pollen Extract Treatment in Summer Hay Fever and Asthma. [In English]

A. W. FRANKLAND. *Acta allergologica* [*Acta allerg. (Kbh.)*] **9**, 183–187, 1955. 7 refs.

A comparison was made between two groups of patients with hay-fever who were treated pre-seasonally with pollen extract to a maximum dose on the one hand of 100 Noon units (low-dosage group) and on the other of 18,000 units (high-dosage group). A previous trial had shown that a maximum dose of 100,000 units gave no advantage over one of 18,000 units. The two groups, each containing 75 patients, were comparable for age and sex. Daily records of attacks were kept through the pollen season.

"Good" results were recorded by 47 patients in the high-dosage group and 12 in the low-dosage group, "moderate" results by 21 in each group, and "poor" results by 42 in the low-dosage and only 5 in the high-dosage group. Of the patients in the high-dosage group, 21 of 29 who also had pollen asthma reported "good" or "moderate" results, compared with 13 of 24 in the low-dosage group. The results both as regards asthma and hay-fever are statistically highly significant. The author concludes that in hay-fever and pollen asthma pre-seasonal treatment aiming at a maximum dose of 18,000 units gives significantly better results than a low-dosage scheme.

R. S. Bruce Pearson

Gastroenterology

78. **Significance of a Furred Tongue**
I. S. L. Loudon. *British Medical Journal* [*Brit. med. J.*] **1**, 18–20, Jan. 7, 1956. 1 ref.

The causes of a furred tongue were investigated in an unselected series of 700 patients seen in general practice. Of these, 100 (including 29 children) who were treated for minor accidents but were otherwise healthy served as controls; 200 of the remainder were children. In all cases the diagnosis, the presence or absence of fever, bowel habits, smoking habits, and state of the teeth were recorded. As regards the control cases the tongue was definitely furred in 12, furred to some degree in 33, and clean in 55. The presence of furring was related to smoking habits, a clean tongue being found in only 8 out of 34 smokers compared with 25 out of 37 non-smokers in this group. A furred tongue was present in 5 out of 9 heavy smokers, but in only 3 out of 15 moderate smokers. Of the 29 children, 22 had a clean tongue and 2 had a definitely furred tongue.

The incidence of furred tongue was higher in patients suffering from infections of the respiratory tract than in the control group, the difference being even more marked when the infection was accompanied by fever. In other infections, with one exception, there was no tendency to furring of the tongue unless fever was present. The exception was infection of the mouth, a furred tongue being observed in all 13 cases, irrespective of fever. Dental caries did not cause furring of the tongue. Diseases of the gastro-intestinal tract, constipation, and diarrhoea were not associated with an increased incidence of furred tongue unless there was fever.

It is concluded that furring of the tongue is due to smoking, respiratory-tract infection, fever (irrespective of cause), or mouth infection. *M. Lubran*

79. **Aetiological Factors in the Pancreatitis Syndrome**
R. A. Joske. *British Medical Journal* [*Brit. med. J.*] **2**, 1477–1481, Dec. 17, 1955. Bibliography.

In 22 out of 90 cases of pancreatitis studied at the Royal Melbourne Hospital the author was unable to find any particular aetiological factor. In the remainder (68 cases) there was some clinical or laboratory evidence of such a factor, and the great importance of "metabolic" causes of pancreatitis, including hyperlipaemia, pregnancy, malnutrition, and haemochromatosis (one case), is stressed. Attention is also drawn to the association between alcoholism and pancreatitis, malnutrition alone probably not accounting for this as small amounts of alcohol may sometimes produce very severe pancreatic pain, suggesting a "trigger" mechanism similar to that seen in Hodgkin's disease.

Vascular disease was regarded as the most important factor in the aetiology of 17 cases, and 10 cases were attributed to a virus infection (hepatitis or mumps). Particular emphasis is laid on the unimportance of gallstone impaction and pancreatic reflux, which were originally suggested as aetiological factors by Halsted and Opie in 1901 on the basis of a single case.

Guy Blackburn

80. **The Geographical Incidence of Chronic Ulcerative Colitis in Britain**
A. G. Melrose. *Gastroenterology* [*Gastroenterology*] **29**, 1055–1060, Dec., 1955. 1 fig., 6 refs.

The author, from the Southern General Hospital, Glasgow, reports an investigation of the geographical variations in the incidence of and mortality from chronic ulcerative colitis, based on the replies to a questionary sent to 30 British teaching hospitals. Analysis of the information received from 23 of these hospitals indicated that the incidence of ulcerative colitis was 10·9 cases per 10,000 hospital admissions and that the case mortality was 12%. The incidence per 10,000 admissions was highest in Manchester (20·2), Oxford (18·2), and London (15·5) and lowest in Newcastle (4·8) and the Scottish towns (6·9). There was "an ill-defined tendency for the incidence to decrease from south to north". The author notes that these figures contrast with the incidence of dysentery, which is much higher in Scotland (65·9 cases per 100,000 population) than in England and Wales (33·1 per 100,000). This evidence suggests that ulcerative colitis is not post-dysenteric in nature.

A. Gordon Beckett

81. **Massive Diverticulosis of the Small Intestine with Steatorrhoea and Megaloblastic Anaemia**
J. Badenoch, P. D. Bedford, and J. R. Evans. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 321–330, Oct., 1955. 6 figs., 21 refs.

In this paper from the Radcliffe Infirmary, Oxford, are reported 5 cases of jejunal diverticulosis with steatorrhea, in 4 of which megaloblastic anaemia was present. Two cases proved fatal, but in neither of these did the authors observe the characteristic atrophy of the entire lymph-node structure of the stomach which is seen in pernicious anaemia, yet in all 5 cases there was a diminished utilization of cyanocobalamin with increased excretion of the orally-administered radioactive vitamin. Intrinsic factor did not increase absorption of cyanocobalamin unless the former was given in much larger doses than those found effective in pernicious anaemia; on the other hand, absorption of radioactive cyanocobalamin was enhanced in 2 cases by short courses of aureomycin. From these findings it is concluded that the megaloblastic anaemia is due to malabsorption of cyanocobalamin caused by much the same mechanism as that responsible for the deficiency of this substance in patients with blind intestinal loops.

Clinically these cases were characterized by rapid onset late in life of abdominal colic, vomiting, fatty diarrhoea, and vitamin deficiency. The differentiation of the con-

dition from idiopathic steatorrhea is based on the late age at onset, the poor response to treatment, and the radiological appearances. The finding of one or more duodenal diverticula is helpful, since the barium-filled jejunal diverticula on the radiograph may be mistaken for the clumping of barium found in idiopathic steatorrhoea.

In most of the published reports of cases of jejunal diverticulosis pain, distension, vomiting, and haemorrhage are considered to be the most important symptoms; diarrhoea is described occasionally, but steatorrhoea not at all. Commenting on this, the authors suggest that diverticulosis with steatorrhoea may have been erroneously diagnosed as idiopathic steatorrhoea.

[They offer no explanation for the sudden onset of symptoms in these patients, who, presumably, had had diverticula without symptoms for many years.]

J. Naish

STOMACH AND DUODENUM

82. Hyperalimentation in the Management of Pyloric Obstruction, with Comments on Certain Theoretical Relationships between Protein Deficiency and Peptic Ulcer

F. P. TURNER. *Gastroenterology* [*Gastroenterology*] **29**, 1061–1068, Dec., 1955. 29 refs.

A regimen for the management of cases of pyloric obstruction which has been used successfully for three years at the Veterans Administration Center, Togus, Maine, is described. It consists essentially in the administration, either by mouth or parenterally, of a high-calorie, high-protein diet, and is based on the theory that protein depletion occurs in patients with pyloric obstruction and is a factor in the aetiology of peptic ulceration. In addition to general treatment with rest, sedation, gastric decompression, and administration of antispasmodics and antacids, the patients receive a minimum daily intake of 75 g. of protein and 1,000 Calories; many are given 100 to 150 g. of protein and 1,500 to 2,000 Calories. In the presence of severe obstruction 2 to 4 litres of protein hydrolysate, usually casein hydrolysate at 38 g. per litre, is given daily, this being sufficient to maintain the patient in positive nitrogen balance.

During the 3-year period an emergency operation for peptic ulcer was necessary in only one case. Subtotal gastrectomy was performed in over 100 cases, with a mortality of 1%; of this number approximately one-quarter came to operation because of pyloric obstruction. At operation there was complete healing of the ulcerative lesions in many cases and a complete absence of inflammation and oedema in the vicinity of the lesion in most. In those cases in which the peptic ulceration was acute and fibrotic stenosis minimal the response to therapy was dramatic, while in those with organic obstruction acute ulcer symptoms were relieved and there was a marked improvement in the degree of gastric retention. In the few patients who responded poorly there was usually severe malnutrition, poor liver function, or haemorrhage.

A. Gordon Beckett

83. Dietetic Treatment of Peptic Ulcer

R. DOLL, P. FRIEDLANDER, and F. PYGOTT. *Lancet* [*Lancet*] **1**, 5–9, Jan. 7, 1956. 10 refs.

The value of a traditional " bland " diet in the treatment of peptic ulcer was studied in two groups of patients at the Central Middlesex Hospital, London. Of the first group of 64 patients with gastric ulcer, 32 received the bland diet and 32 an " almost normal " diet. The criteria for evaluation were the frequency of symptoms during one month's treatment and the change in ulcer size and the gain in weight at the end of that period. No significant difference was observed between the two groups in the extent of healing of the ulcer. The patients on the control diet gained twice as much weight as those on the bland diet; on the other hand about twice as many patients on the bland diet as on the control diet were free from pain.

In the second group of 130 out-patients, 80 with gastric and 50 with duodenal ulcer, the effect of the two diets was judged from the radiological appearances after one year's treatment and the incidence of pain and dyspepsia during that time. The radiological findings indicated that the patients with gastric ulcer did rather better on the control diet and patients with duodenal ulcer did better on the bland diet, but the differences were small and probably not significant. Symptomatic relief was the same with both diets.

It is concluded that the traditional bland diet has no merit over the more liberal, almost normal, control diet in patients with peptic ulcer. The greater incidence of symptoms among in-patients on the control diet was probably of psychological origin and due to mistrust of the unconventional treatment.

R. Schneider

84. Subtotal Gastrectomy for Peptic Ulcer. A One to Four and One-half Year Clinical and Laboratory Follow-up Study

P. B. METCALF, P. COOPER, and R. H. SMITHWICK. *Annals of Surgery* [*Ann. Surg.*] **142**, 924–937, Dec., 1955. 5 figs., 31 refs.

The results of subtotal gastrectomy for peptic ulcer were assessed in 269 consecutive cases operated on at the Veterans Administration Hospital, Providence, Rhode Island, the period of follow-up being one year to 4½ years. In all the cases two-thirds to three-quarters of the stomach was resected, and a Billroth-II type of anastomosis was performed. The over-all mortality was 1·9%, which compares favourably with the mortality in other published series. Postoperative complications are analysed in detail; minor complications occurred in 9·2% and major complications in 15·3% of cases.

Of the original 269 patients, 201 reported for follow-up examination, and the incidence of late sequelae, which included weight loss, dumping syndrome, disturbed meal pattern, mechanical symptoms, gastrojejunal ulceration, and decreased working capacity, was assessed. A disturbed meal pattern, indicated by such factors as diminished food intake, excessive " obligatory feedings ", specific food intolerances, and poor appetite, proved to be the most common and distressing side-effect. Gastrojejunal ulceration was suspected in 18 patients. Gastric

secretion was studied in 172 of the patients at the time of the follow-up investigation. A striking difference was observed between the patients with duodenal ulcer and those with gastric ulcer in the response to insulin stimulation, 39% of the former and only 6% of the latter producing free acid. In all 9 patients with proven or probable late postoperative gastrojejunal ulceration there was free acid in some phase; 6 of these secreted more than 5 mEq. per hour, compared with slightly more than a quarter of the whole duodenal-ulcer group.

R. G. Rushworth

85. Cancer Development in the Gastric Stump after Partial Gastrectomy for Ulcer

N. HELSINGEN and L. HILLESTAD. *Annals of Surgery* [*Ann. Surg.*] **143**, 173–179, Feb., 1956. 1 fig., 13 refs.

86. The Pain of Peptic Ulceration

A. W. M. SMITH. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 393–407, Oct., 1955. 2 figs., 33 refs.

In the literature three main theories concerning the origin of the pain of peptic ulceration have been advanced: (1) the acid theory, which ascribes the pain to irritation of the ulcer base by the acid of the gastric juice; (2) the " motility theory ", which relates the pain to the muscular activity, normal or abnormal, of the stomach or duodenum; and (3) the theory that ulcer pain is caused directly by the inflammatory reaction around the ulcer.

At Edinburgh University the author studied the relationship between pain and motility and acidity in 28 patients with typical peptic-ulcer pain, a balloon-kymograph technique being used to record gastric and duodenal motility. Radiological examination of 27 of the patients revealed a duodenal ulcer in 16, an ulcer deformity of the duodenal cap in 3, gastric ulcer on the lesser curvature in 6, and prepyloric scarring in one case; in the remaining case the findings were negative. Spontaneous attacks of pain were experienced by 17 patients; the pain occurred concomitantly with the presence of free acid in the gastric juice in 15 and in the absence of free acid in 2. A close correlation between the attacks and changes in gastric acidity was found in only 3 cases in this group and partial correlation in 4; in the remainder the pain was not related to levels of acidity.

Injection into the stomach of 100 ml. of a 0·5% solution of hydrochloric acid caused pain in 12 out of 19 patients after a single injection and in 3 more after a second injection; pain developed in all of the 6 patients who had a gastric ulcer, the average interval between injection and onset of pain being 8·8 minutes; pain developed in 9 of the 13 with a duodenal lesion after an average interval of 7·2 minutes. Injection of 30 to 100 ml. of 0·5% hydrochloric acid into the duodenum of 5 patients who had scarring or ulceration of the duodenum caused pain in each case after an average interval of 3½ minutes. Finally, injection of 30 to 60 ml. of a 9% solution of sodium bicarbonate into the stomach on 18 occasions and into the duodenum on 6 occasions was followed by relief of pain after an average delay of 9 minutes.

Throughout this investigation there was poor correlation between changes in motility and (*a*) spontaneously occurring pain, (*b*) artificially induced pain, and (*c*) relief of pain following injection of sodium bicarbonate.

The author considers the results to indicate that " the sensitivity of the ulcer is much more important than any particular level of acid or degree of motility ".

Joseph Parness

87. Duodenal Biopsy

M. SHINER. *Lancet* [*Lancet*] **1**, 17–19, Jan. 7, 1956. 7 figs., 5 refs.

A modification of the gastric biopsy tube whereby it is possible to obtain specimens of the duodenal mucosa is described in this paper from the Postgraduate Medical School of London. With this tube duodenal biopsy was successful in 12 out of 19 cases in which it was attempted. There were no complications. The character of the specimens varied with the site of aspiration; in the more distal parts of the duodenum the villi became longer and thinner, the muscularis mucosae thicker, and Brunner's glands were no longer seen. [So far no attempt has been made to utilize this method for diagnostic purposes.]

R. Schneider

88. A Duodenal-ulcer Family

J. T. WRIGHT, A. GRANT, and D. JENNINGS. *Lancet* [*Lancet*] **2**, 1314–1318, Dec. 24, 1955. 1 fig., 13 refs.

The occurrence of duodenal ulcer in two branches of a family (first cousins) was studied at the London Hospital. Of 13 living siblings in " K " branch, 9 had evidence of duodenal ulceration, while 6 uncles were reported to have died from gastro-intestinal disease. Branch " J " had 4 members, 2 of whom had duodenal ulcer; the father also had a duodenal ulcer.

The authors analysed the various circumstances which might have determined which members of the families should develop ulceration, but inquiry concerning domestic habits, psychological stress, and occupation did not reveal any relevant predisposing or aggravating factors. Examination of the blood groups gave equivocal results.

T. J. Thomson

89. Continuous Intragastric Milk Drip in Treatment of Uncomplicated Gastric Ulcer

R. DOLL, A. V. PRICE, F. PYGOTT, and P. H. SANDERSON. *Lancet* [*Lancet*] **1**, 70–73, Jan. 14, 1956. 1 fig., 15 refs.

An investigation into the healing of gastric ulcer was carried out jointly at the Central Middlesex and St. Mary's Hospitals, London. A group of 82 patients with gastric ulcer received the standard medical treatment and a continuous intragastric milk drip, with and without the addition of sodium bicarbonate. To 72 of them 6 pints (3·4 litres) of milk was given every 24 hours, administration being continuous day and night, for 2 weeks, and then 2 pints at night only for a further 10 days; in 10 cases the milk was given day and night for 3 weeks. Sodium bicarbonate was added to the milk drip, 40 g. to each 6 pints in 40 cases and 80 g. and 140 g. respectively in 2; in the remaining 40 cases

no alkali was given. The results in these 82 cases were compared with those obtained in 82 controls given the standard medical treatment but not the milk drip, the two groups being similar in all essential respects. The rate of healing was assessed by comparing the size of the ulcer as revealed on radiographs taken before treatment started and again at the conclusion.

No significant difference between the two groups in the rate of healing could be demonstrated, ulcers being healed at the end of one month in 20 out of 82 cases in each group. It did appear, however, that pain was relieved more rapidly in patients given the milk drip than in those who were not, and that the former gained more weight than the controls. *T. D. Kellock*

90. Continuous Intragastric Milk Drip in the Treatment of Upper Gastro-intestinal Haemorrhage

A. M. DAWSON. *Lancet* [*Lancet*] **1**, 73–74, Jan. 14, 1956. 3 refs.

The value of a continuous intragastric milk drip in the prevention of recurrent upper gastro-intestinal haemorrhage was studied at the Central Middlesex Hospital, London. In alternate cases out of a consecutive series of 100 a continuous drip of non-citrated milk (6 pints (3·4 litres) in 24 hours) was given for the first 72 hours after admission. The stomach was aspirated hourly and the contents examined for fresh or altered blood; the pulse rate was recorded hourly and the blood pressure 4-hourly. There was no significant difference between the two groups in the incidence of further haemorrhage; only in one case did aspiration give warning of massive haemorrhage before other clinical signs were apparent.

T. D. Kellock

LIVER

91. Changes in the Finger-nails in Cirrhosis of the Liver as a Result of Altered Peripheral Circulation. (Über Fingernagelveränderungen bei Lebercirrhose als Folge veränderter peripherer Durchblutung)

G. A. MARTINI and J. E. HAGEMANN. *Klinische Wochenschrift* [*Klin. Wschr.*] **34**, 25–31, Jan. 1, 1956. 6 figs., 43 refs.

Clubbing of the fingers has been recognized since the time of Hippocrates as a sign of chronic lung disease, but it is also found in various other chronic diseases which appear to have no features in common. Its occurrence in cirrhosis of the liver is generally regarded as rare, and those cases reported in the literature are almost exclusively of biliary cirrhosis of the Hanot type.

The present authors, working at the University Hospital, Hamburg–Eppendorf, noticed that in many cases of erythema palmaris in patients with cirrhosis the erythema extended to the dorsal part of the terminal phalanx and the borders of the nails, while not infrequently there was also an "hour-glass" deformity of the nails which they regard as representing a slight degree of clubbing. It was shown by Mendlowitz in 1938 that in cases of finger-clubbing associated with chronic pulmonary disease the blood flow in the terminal phalanx was increased and the arterial pressure markedly elevated. The authors have therefore studied three groups of subjects—a control group of 18 healthy subjects and patients without chronic disease, 8 patients with clubbing of the fingers due to chest disease (tuberculosis or bronchiectasis), and 27 patients with liver disorders of various kinds (mostly cirrhosis)—in order to determine whether patients suffering from cirrhosis, with or without changes in their nails, showed the same circulatory changes, the possibility being visualized that changes in the circulation precede those in the nails.

Calorimetric estimations of the peripheral circulation were carried out on the fingers, the other arm being warmed to exclude sympathicotonic influences on the vessels, and arterial tension was measured in the fingers with the Gärtner tonometer. By these methods it was confirmed that the blood flow in the terminal phalanx of clubbed fingers was higher than in normal fingers and it was also shown to be considerably increased in the fingers of patients suffering from cirrhosis of the liver whether or not any change was visible in the nails. Thus the mean blood flow in ml. per c.cm. of finger tissue per minute in healthy persons was $0{\cdot}66 \pm 0{\cdot}06$, in the patients with pulmonary disease $0{\cdot}804 \pm 0{\cdot}123$, and in 16 cases of cirrhosis $0{\cdot}875 \pm 0{\cdot}105$. The digital arterial blood pressure was similarly increased in almost every case.

The relation of these findings to the pathogenesis of finger-clubbing and of other changes found in the nails in cirrhosis is discussed. *E. Forrai*

92. Treatment of "Hepatic Coma" with L-Glutamic Acid

W. V. MCDERMOTT, J. WAREHAM, and A. G. RIDDELL. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 1093–1102, Dec. 22, 1955. 7 figs., 39 refs.

At the Massachusetts General Hospital, Boston, 28 patients with hepatic coma were given L-glutamic acid by mouth or intravenously in a dosage of 25 g. daily usually for 2 or 3 days. In one group of 6 patients with severe liver-cell failure in whom ammonia intoxication seemed to be only one of many metabolic disturbances treatment was ineffective, although the blood ammonia level fell in some instances. In a second group of 14 patients coma was precipitated by some exogenous factor, usually gastro-intestinal haemorrhage. Ammonia intoxication was the principal abnormality, and after administration of L-glutamic acid the blood ammonia level fell and the mental state often improved. [Rapid spontaneous improvement may occur in these cases without specific treatment.] The remaining 8 patients suffered from compensated liver disease and a chronic confused state which seemed to be due mainly to ammonia intoxication. With treatment there was usually a fall in the blood ammonia level and an improvement in the mental state of the patients, but cessation of treatment was followed by relapses.

[There is little evidence that glutamic acid was life-saving in any of these cases, but few will quarrel with the contention that there is more than one type of "hepatic coma".] *P. C. Reynell*

Cardiovascular System

93. Anticoagulant Therapy in Idiopathic Occlusion of the Axillary Vein

J. MARKS. *British Medical Journal* [*Brit. med. J.*] **1**, 11–13, Jan. 7, 1956. 15 refs.

The author, from the University of Cambridge, reports 12 cases of idiopathic occlusion of the axillary vein (Paget–Schroetter syndrome) and reviews 19 cases in the literature with special reference to the value of anticoagulants in treatment. He states that the cases fall into two distinct groups—those in which from the onset there is considerable pain and those in which pain is absent or very slight. Cases in the former group respond very satisfactorily to anticoagulant therapy, and it is suggested that the condition here is due to a primary thrombophlebitis of the axillary vein. In the second group of cases there is little improvement from anticoagulants and the author attributes the condition to extravascular obstruction, with perhaps subsequent venous thrombosis. *P. D. Bedford*

94. Direct Vision Intracardiac Surgery by Means of a Reservoir of "Arterialized Venous" Blood

H. E. WARDEN, R. C. READ, R. A. DEWALL, J. B. AUST, M. COHEN, N. R. ZIEGLER, R. L. VARCO, and C. W. LILLEHEI. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **30**, 649–657, Dec., 1955. 1 fig., 16 refs.

Experience gained by the authors at the University of Minnesota Hospitals, Minneapolis, with the controlled cross-circulation technique as a means of by-passing the heart during open cardiac surgery in over 40 cases has shown that (1) a perfusion rate representing only a small fraction of the basal cardiac output is sufficient to prevent damage to the central nervous system, liver, and kidneys, and (2) a long period of perfusion is not usually required, as in most cases the intracardiac part of the operation can be completed under direct vision within 15 minutes. Thus, especially in infants and small children, the total amount of blood exchanged during the perfusion period is relatively small, and it has been found possible to provide this from a reservoir instead of a donor. The principle of the technique is unchanged, the circulation being maintained by means of a simple pump which simultaneously delivers oxygenated blood to the patient's arterial system and withdraws an equal volume of venous blood from the vena cava. If the arm is first heated by placing it in a water bath at 45 to 47° C. for 15 to 20 minutes the blood withdrawn from the antecubital vein is strikingly similar to arterial blood. Thus the removal of a large volume of blood from an artery of a single donor, which necessitates the simultaneous transfusion of an equal volume of citrated blood into a vein, can be avoided and contributions of "arterialized" venous blood obtained from several donors. The blood is heparinized (20 mg. of heparin to 500 ml. of blood) and is kept in a water bath at 38° C. or, if not required immediately, stored at 4° C. and warmed before use. The volume of blood required for a given operation is determined by the flow-rate required, the weight of the patient, and the estimated length of perfusion required.

This method of reservoir perfusion, with total by-pass of the heart and lungs for as long as 45 minutes, has been used successfully on 5 patients with various types of intracardiac defect. A report is given of the first case so treated, that of an infant of 6 months weighing 4·8 kg. with a high ventricular septal defect. Total by-pass was maintained for the 14¾ minutes needed to close the defect under direct vision, and during this time 2,225 ml. of blood was perfused out of a total of 4,000 ml. available. The infant made an uninterrupted recovery and was thriving 6 months later, when no cardiac murmurs were audible. *F. J. Sambrook Gowar*

95. Long-term Outlook for Healed Subacute Bacterial Endocarditis

C. E. MENDELSON, A. CAHUÉ, L. N. KATZ, and W. A. BRAMS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 437–441, Feb. 11, 1956. 16 refs.

The administration of antibiotics in subacute bacterial endocarditis has reduced the immediate mortality to about 25%; in a further 6 to 11% of cases death occurs later from cardiac failure, making the over-all mortality 31 to 36%. The present authors have endeavoured to determine the effect of bacterial endocarditis on the cardiac lesions in the survivors by means of a follow-up study of 17 patients successfully treated at the Michael Reese Hospital, Chicago, between 1944 and 1947. Of these 17 patients, 4 had underlying congenital heart disease, 11 had rheumatic valvular disease, and one had syphilitic valvular disease; in one patient no lesion was found. In all cases positive blood cultures confirmed the diagnosis, and treatment was with penicillin.

During the period of observation 7 of the patients died, one after a recurrence of endocarditis. Of the remaining 10 patients, 7 were asymptomatic for 7½ to 10 years after the infection, but 3 showed evidence of cardiovascular deterioration. Analysis of the group of 7 fatal cases revealed that the cardiac lesions present before endocarditis developed were more severe than in patients who survived, 5 having had significant aortic incompetence. Moreover, the average age of the patients at the time of infection was higher in this group than in survivors. Patients in whom the initial cardiac lesions were slight did not appear to deteriorate further as the result of the attack of subacute bacterial endocarditis.

The authors conclude that the prognosis is less favourable in aortic valvular disease and in older patients.

[The total dosage of penicillin given seems very small by modern standards; 11 patients each received a total

of less than 10,000,000 units. However, there was no very striking difference in this respect, apparently, between those patients who survived and those who died.]

F. Starer

96. **Myocardial Toxoplasmosis**

J. W. PAULLEY, R. JONES, W. P. D. GREEN, and E. P. KANE. *British Heart Journal* [*Brit. Heart J.*] **18**, 55–64, Jan., 1956. 9 figs., 23 refs.

The authors present further information (in the form of photographs, photomicrographs, electrocardiographic tracings, and additional post-mortem findings) on the 4 cases of myocardial toxoplasmosis previously reported (*Lancet*, 1954, **2**, 624; *Abstracts of World Medicine*, 1955, **17**, 116) which were seen at the East Suffolk and Ipswich Hospital because of cardiac symptoms, and in which blood tests for toxoplasmosis gave positive results. The cases are described as before, with the addition of the later findings.

The authors suggest that the predominant myocarditis in these cases may be due to a strain of *Toxoplasma* with a specific affinity for the heart, and that this possibility should be considered in all forms of obscure myocarditis, and especially in cases of familial cardiomegaly and idiopathic hypertrophy.

[These findings are of great importance and worthy of record. It is to be noted, however, that in none of the histological specimens was the organism demonstrated. It is difficult also to explain the long history and familial incidence in the presence of positive complement-fixation reactions, if these are accepted as evidence of a recent infection.] *H. G. Farquhar*

DIAGNOSTIC METHODS

97. **The Intracardiac Electrogram as an Aid in the Localization of Pulmonary Stenosis**

D. EMSLIE-SMITH, K. G. LOWE, and I. G. W. HILL. *British Heart Journal* [*Brit. Heart J.*] **18**, 29–34, Jan., 1956. 7 figs., 4 refs.

The first-named author has already shown (Emslie-Smith, *Brit. Heart J.*, 1955, **17**, 219; *Abstracts of World Medicine*, 1955, **18**, 292) that the intracardiac "electrogram" (IEG) recorded from an electrode at the tip of a cardiac catheter lying in the pulmonary artery differs from that obtained when the tip lies in the right ventricle. The change in the electrogram usually occurs abruptly, as can be seen in a continuous recording made as the catheter tip is pulled back from the pulmonary artery into the right ventricle. The authors have therefore used this method together with pressure pulse recordings as a means of identifying the point of passage through the pulmonary valve for detecting the site of stenosis during the investigation at Dundee Royal Infirmary (University of St. Andrews) of 43 patients with heart disease.

Excluding a few cases in which extrasystoles marred the record, there were 19 cases of pulmonary stenosis, of which 15 appeared to be cases of simple valvular stenosis, 3 of Fallot's tetralogy with valvular stenosis, and one of infundibular stenosis. The presence of valvular stenosis was indicated by a simultaneous change in form in the IEG and rise in pressure as the catheter tip was withdrawn through the stenosed valve into the ventricular cavity.

[Although anatomical confirmation of the diagnosis was apparently obtained in only a few of these cases, the method described seems likely to be of practical help in the interpretation of catheter findings.]

J. A. Cosh

98. **Paradoxical Splitting of the Second Heart Sound**

I. R. GRAY. *British Heart Journal* [*Brit. Heart J.*] **18**, 21–28, Jan., 1956. 6 figs., 9 refs.

Some workers have observed that normally the splitting of the second heart sound becomes more marked on inspiration. This is explained by the increased filling of the right atrium and ventricle during inspiration, with a consequent prolongation of right ventricular systole. Sometimes, however, a clearly split second sound becomes single or more closely split in inspiration. This paradoxical behaviour is due to reversal of the normal order of valve closure, pulmonary closure preceding aortic closure. This phenomenon was studied by means of phonocardiography in 40 cases at the Institute of Cardiology, London.

Paradoxical splitting of the second heart sound was observed in 18 out of 21 cases of left bundle-branch block; in these it was clearly due to delay in the onset of activation of the left ventricle. The same phenomenon was noted in 10 out of 23 cases of aortic stenosis, and in these it was due to prolongation of left ventricular systole in association with a shortened right ventricular systole; it was generally a sign of severe stenosis. Paradoxical splitting of the second sound was present in 10 out of 29 cases of patent ductus, the mechanism being the same as in aortic stenosis. It was heard in only 2 out of 11 cases of severe pulmonary hypertension with balanced or reversed shunt; it was present, however, in 8 out of 15 cases of left-to-right shunt. Paradoxical splitting of the second sound was also recorded in one case each of hypertensive heart disease and mitral stenosis, but it was absent from 10 further cases of each of those conditions. *C. Bruce Perry*

99. **The Splitting of Heart Sounds. A Spectral Phonocardiographic Evaluation of Clinical Significance**

V. A. MCKUSICK, W. P. REAGAN, G. W. SANTOS, and G. N. WEBB. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 849–861, Dec., 1955. 6 figs., 21 refs.

The authors have investigated, at Johns Hopkins Hospital and Medical School, Baltimore, the significance of splitting of the heart sounds by means of a sound spectrograph, which records the intensity and frequency (that is, the pitch) of the sounds; simultaneous electrocardiographic tracings were made for timing purposes. From an initial study of the normal heart sounds they conclude that possible components of the first heart sound are: (1) ventricular vibrations in response to a trial contraction; (2) closure of the atrio-ventricular (A–V) valves; (3) vibrations produced by the contracting myocardium; (4) opening of the arterial valves;

and (5) ejection vibrations. The second sound may be caused by: (1) myocardial relaxation; (2) closure of the arterial valves; (3) the water-hammer phenomenon in the arteries; and (4) opening of the A–V valves.

Split sounds are fundamentally due to asynchronism in the closing of the valves. This may arise from some abnormality in the propagation of the impulse (for example, bundle-branch block, ventricular extrasystoles, or idioventricular rhythm) or may be due to mechanical defects either causing discrepancy in ventricular stroke volumes (as in atrial septal defect) or resulting in different rates of ejection (as in mitral and aortic regurgitation). Hypertension did not appear to cause splitting. In a patient over the age of 40 with an otherwise normal heart marked inspiratory splitting of the sounds is suggestive of respiratory disease which is causing a greater "negative intrapleural pressure" than normal. A recording of the effect of respiration on split sounds can also help to differentiate the various types of heart block and to exclude conditions simulating split heart sound.

Adventitious sounds which may be confused with a split first sound are: (1) normal atrial sound, (2) presystolic gallop, (3) a protosystolic click, due to a dilated pulmonary artery, to disease of the ascending aorta, or to pericardial adhesions. Those which may be mistaken for a split second sound are: (1) telesystolic click due to pericardial adhesions, (2) a mitral opening snap, (3) a normal third heart sound, (4) protodiastolic gallop, and (5) the isodiastolic snap of constrictive pericarditis.

The authors conclude, however, that in view of the frequent observation of splitting in the normal heart the study of this phenomenon is of limited diagnostic value, especially in children. It is of more significance when it is exaggerated with expiration (as in left bundle-branch block), when it persists through all phases of respiration (as in atrial septal defect), or when there is no respiratory disease. *D. Goldman*

100. Diagnostic Value of Phonocardiography in Mitral Stenosis. Mode of Production of First Heart Sound

J. J. KELLY. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 862–868, Dec., 1955. 3 figs., 26 refs.

The author describes several changes of diagnostic significance observed in the phonocardiograms of patients with mitral stenosis who were examined by means of a twin-beam phonocardiograph, the recordings of which were related to simultaneous electrocardiograms, at Kings County Hospital Center, Brooklyn, New York. The time elapsing between the Q wave and the first heart sound was recorded in 75 patients with mitral stenosis and compared with that in 100 cases of heart disease other than mitral stenosis. The mean interval was 0·06 second in the mitral group and 0·04 second in the other group. It was shown that the degree of delay was proportional to the severity of the stenosis and was significantly shortened by successful commissurotomy. This delay of the first heart sound is of particular diagnostic value since it is usually most marked when the typical murmurs are absent. The author believes that the delay is due to the disparity between the end diastolic pressures in the left atrium and left ventricle, and that the sound does not occur until the ventricular pressure has become equal to the atrial pressure.

The study further showed that there was an opening snap of the mitral valve in 72 out of the 75 patients with mitral stenosis, but in only one of the other patients. This finding is of significance as it was observed more frequently in cases of severe mitral stenosis than was a diastolic murmur. Details of the pre- and post-operative findings in 16 of the patients are given. It appears that the interval between the second sound and the opening snap is inversely related to the severity of the stenosis, and that this interval lengthens with successful mitral surgery. The author concludes with a discussion of the components of the first sound and the mechanism of the opening snap. *D. Goldman*

CONGENITAL HEART DISEASE

101. Congenital Heart Block

M. CAMPBELL and M. G. THORNE. *British Heart Journal* [*Brit. Heart J.*] **18**, 90–102, Jan., 1956. 8 figs., 33 refs.

A follow-up report, covering a period of 25 years, of 7 cases of congenital complete heart block is presented in this paper from Guy's Hospital and the Institute of Cardiology, London. Since the report was first prepared one of the patients has died from an obscure cardiovascular condition; the remaining 6 are doing well. In one, sinus rhythm with latent heart block has developed and in another there is enlargement of the heart with evidence of an additional lesion. The remaining patients have systolic murmurs which are thought to be functional or cardio-respiratory. The heart rate (40 to 50 per minute) is faster than in cases of acquired heart block; there is no tendency for blood pressure to rise with age. Apart from the block the electrocardiogram is generally normal.

The authors also describe 8 cases, seen in the last few years, of heart block with manifest congenital heart disease. In 3 cases in this group the block was not always complete, 2:1 block or latent block with dropped beats being seen at times. When the block was complete the ventricular rate was even faster—50 to 70 per minute—than it was in the group of patients without congenital abnormalities. In these cases the prognosis is that of the associated lesion and is not greatly affected by the presence of the heart block. *T. Semple*

102. The Influence of Age on the Haemoglobin Level in Congenital Heart Disease

R. J. SHEPHARD. *British Heart Journal* [*Brit. Heart J.*] **18**, 49–54, Jan., 1956. 2 figs., 18 refs.

The author discusses variations in the haemoglobin level with age observed at Guy's Hospital, London, in 350 patients, aged 2 to 60 years, suffering from congenital heart disease, of whom 184 were cyanotic and 166 were not. The haemoglobin content of the blood was assessed by measuring its oxygen capacity, the dividing line between cyanotic and acyanotic cases being taken as an oxygen saturation of 94% when the patient was unanaesthetized and 92% when anaesthetized.

The patients were grouped according to age, the mean haemoglobin content for cyanotic and acyanotic cases determined in each age group, and curves plotted showing the relationship between age and haemoglobin level. On comparison with a similar curve for normal children derived from the results of an M.R.C. survey, the curve for acyanotic cases was at a lower level, but climbed more steeply than the normal curve. The curve for cyanotic cases, however, lay at a much higher level up to the age of 20, when it began to fall off rapidly so that the difference had almost disappeared by the age of 40—probably owing in part to the death of the most severely ill patients. The author considers that 85% of congenital heart disease in children can be recognized as belonging to the " cyanotic " type on this criterion alone.

A comparison of the oxygen capacity of the acyanotic cases with those reported in the survey carried out by the Medical Research Council in 1945 indicated a greater deficiency of haemoglobin in the present series of patients which, the author suggests, might be amenable to iron therapy. This factor may be of even greater importance in cyanotic cases. *H. G. Farquhar*

CHRONIC VALVULAR DISEASE

103. Disability and Circulatory Changes in Mitral Stenosis

H. E. Holling and A. Venner. *British Heart Journal* [*Brit. Heart J.*] **18**, 103–122, Jan., 1956. 3 figs., 38 refs.

The authors present, from Guy's Hospital, London, the results of a careful analysis of the circulatory changes in 81 patients (27 men and 54 women) with uncomplicated mitral stenosis. The patients, who were all in the 3rd, 4th, and 5th decades of life, were divided into five groups according to the degree of physical disability present, ranging from " no disability " to breathlessness and fatigue on very slight activity.

They have found that measurement of pulmonary arterial pressure offers a good means of discriminating between all groups, and that determination of the oxygen saturation of the mixed venous blood discriminates clearly between the three most severe grades. Cardiac output showed some reduction with increasing disability, but the relationship was not very exact. The height of pulmonary " capillary " pressure was similar in the three most disabled groups, whereas pulmonary arterial pressure differed significantly from group to group. The degrees of depression of oxygen saturation of mixed venous blood and of elevation of pulmonary arterial pressure were shown to be fairly closely related. In discussion they state that when mitral stenosis is complicated by cardiac neurosis investigation will indicate a degree of disability less than expected; similarly, when the stenosis is associated with chronic respiratory disease pulmonary arterial pressure will be as high as in uncomplicated cases, but pulmonary " capillary " pressure will be lower. No satisfactory method of distinguishing the effects of mitral regurgitation has been demonstrated.

Cardiac catheterization after successful valvotomy showed in some cases evidence of persisting pulmonary vascular changes. The authors point out that in cases of mitral stenosis cardiac catheterization is necessary only when the exact diagnosis is uncertain or when the significance of the signs of complications is not apparent. In uncomplicated cases the results of catheterization merely support the clinical diagnosis. *T. Semple*

104. Circumferential Suture of the Mitral Ring

J. C. Davila, R. P. Glover, R. G. Trout, F. S. Mansure, N. E. Wood, O. H. Janton, and B. D. Iaia. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **30**, 531–563, Nov., 1955. 16 figs., 13 refs.

Most operations designed to correct mitral incompetence have involved the replacement of the damaged valve by foreign materials introduced into the lumen of the heart. Such operations entail much intracardiac manipulation and are frequently followed by intracardiac thrombosis and embolism. Moreover, they reduce the size of the effective valvular orifice. In a large proportion of cases of combined mitral stenosis and incompetence there is a significant degree of annular dilatation which places the cusps under severe tension and further hampers their movement. The operation described in this paper from the Presbyterian Hospital in Philadelphia is designed to reduce the size of the atrio-ventricular ring by circumferential suture (with or without valvotomy), thus enabling the cusps to function more efficiently. It entails minimal intracardiac manipulation and is applicable to most forms of mitral incompetence, except where the valve is rigid and solidly calcified.

The technique was worked out in numerous preliminary experiments on dogs, in which the effects and fate of the suture were observed. The suture is passed through the base of the inter-atrial septum and into the A-V groove, passing deep to the coronary vessels, and is tied in front just to the left of the anterior descending branch of the left coronary artery, with a finger in the left atrium as a guide. The most satisfactory of the suture materials tried was braided cotton umbilical tape. In 18 of a group of 25 animals surviving the operation in its original form the suture cut through the tissues and eroded into the lumen of the left atrium, either rapidly, with rupture of the heart, or gradually, with projection of the suture into the lumen and formation of granulations on it. The erosion always occurred in the segment adjacent to the transverse sinus, and was avoided in later experiments by covering this part of the suture with a free graft of pericardium. [For details of the operative technique the original paper should be consulted.]

The operation has been performed on 7 patients severely ill with mitral incompetence; 4 have survived and show some improvement, but the follow-up period has been too short for a proper assessment of the results. There was one operative death, and 2 patients died within 3 months of operation. It is claimed that the procedure is relatively simple and safe and, when properly performed, causes no significant damage to the conducting tissue, the coronary circulation, or the myocardium, and does not cause mitral stenosis. The authors consider that further clinical trial is justified, but that for the

present the operation should be performed only on critically ill patients. It is emphasized that a preliminary study of the anatomy of the region and practice on experimental animals are essential to the proper performance of the operation. *F. J. Sambrook Gowar*

105. Mitral Commissurotomy Performed during Anticoagulant Prophylaxis with Dicumarol

O. STORM and A. TYBJÆRG HANSEN. *Circulation* [*Circulation (N.Y.)*] **12**, 981–985, Dec., 1955. 1 fig., 17 refs.

In an effort to lessen the risk of thrombo-embolic accidents the authors have performed mitral valvotomy under cover of an anticoagulant (dicoumarol) in 26 cases operated on at the Rigshospital, Copenhagen. They have found that there is little risk of haemorrhage if the prothrombin level, which is determined daily, is kept above 10%. Dicoumarol, the maintenance dose of which was determined by the response obtained, was given for a 5-week period, starting 2 weeks before the operation. The postoperative blood loss through the drainage tubes was found to be no greater in patients on this regimen than in the 26 similar patients in the control group who did not receive the drug. A surprisingly high proportion of the control group (6 out of 26) experienced postoperative thrombotic incidents, but none of the patients given the anticoagulant did so. It is admitted that no definite conclusion can be drawn from this small study, but the method seems promising and the risk of uncontrollable haemorrhage occurring is considered to be slight, provided appropriate precautions are taken. *J. R. Belcher*

106. Mitral Commissurotomy in Cases in which Approach through the Left Auricular Appendage is Impossible. (La commissurotomia mitralica in casi di impossibilità all'impiego dell'appendice auricolare di sinistra)

P. L. BRUZZONE and G. GUGLIELMINI. *Minerva chirurgica* [*Minerva chir. (Torino)*] **11**, 45–50, Jan. 31, 1956. 5 figs., bibliography.

The normal surgical approach to the mitral valve through the left auricle is rendered impossible by hypoplasia of the appendage, fragility of its muscle, obliteration of its cavity by scarring or thrombosis, calcification of the parietes, or excision of the appendage at a previous operation. In only 3 out of a series of 500 cases in which commissurotomy was performed by Dogliotti at the University Cardiac Surgical Centre, Turin, was an alternative approach to the stenotic valve necessary, the route chosen being via the left superior pulmonary vein in each case, although various others are available.

In the presence of a relatively small degree of hypoplasia of the auricular appendage valvotomy may be performed by means of a rubber-protected clamp, the Bailey dilator, or the small finger of the left hand. When the appendage is minute or deficient, however, a transatrial route is possible, or if a right thoracotomy is being performed the right pulmonary vein can be used. Alternatively, an artificial appendage created from fascia lata can be sutured to the atrium, while an approach to the mitral valve through the ventricular muscle has occasionally been used. The more common route of access through the left superior pulmonary vein proved quite successful in the 3 cases in the present series. This method is described in detail, its advantages and disadvantages being enumerated. *C. A. Jackson*

107. Incidence of Asymptomatic, Active Rheumatic Cardiac Lesions in Patients Submitted to Mitral Commissurotomy and the Effect of Cortisone on These Lesions. Clinical and Histopathologic Study of Sixty Cases

J. R. GIL, H. RODRIGUEZ, and J. J. IBARRA. *American Heart Journal* [*Amer. Heart J.*] **50**, 912–920, Dec., 1955. 7 figs., 16 refs.

The incidence of lesions of active rheumatic fever in the auricular appendage at the time of mitral commissurotomy was studied in 60 patients at the National Institute of Cardiology, Mexico City. Cortisone was given to 14 of the patients before and after operation. Histologically, the cases were divided into three groups: (1) those in which there were Aschoff nodes, cellular infiltration, and fibrinoid necrosis; (2) cases similar to (1) but without fibrinoid necrosis; and (3) cases in which Aschoff nodes were observed, but there was no fibrinoid necrosis or acute cellular infiltration. Two healing stages with fibrosis were recognized. On the basis of these criteria, 36 of the 60 patients showed rheumatic activity, 9 showed signs of healing, and 15 had healed lesions. Active rheumatic lesions were infrequent and less severe in the cortisone-treated patients than in the controls. Relapse occurred after operation in some of the cases in both the treated and untreated groups, but the authors nevertheless consider that the effect of cortisone on the prevention of these relapses merits further study.

[The statement that " it is certain that cortisone has a beneficial effect on rheumatic active lesions " is not warranted by the results of this investigation.]

G. Loewi

DISTURBANCES OF RHYTHM AND CONDUCTION

108. Use of External Electric Pacemaker in Cardiac Arrest

P. M. ZOLL, A. J. LINENTHAL, L. R. NORMAN, M. H. PAUL, and W. GIBSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1428–1431, Dec. 10, 1955. 1 fig., 10 refs.

The authors describe, from Beth Israel Hospital (Harvard Medical School), Boston, the resuscitation of 27 patients in cardiac arrest associated with Stokes–Adams attacks by means of an electric cardiac pacemaker externally applied. In 24 cases there was ventricular standstill and in 3 slow idioventricular rates. Stokes–Adams attacks which were due to ventricular tachycardia or fibrillation were not stopped by use of the pacemaker. In some of the successful cases stimulation was continued for periods as long as 109 hours. [There is no description of the pacemaker, which was, however, described in a previous paper (*Circulation*

(*N.Y.*), 1954, **9**, 482; *Abstracts of World Medicine*, 1954, **16**, 385).]

The authors suggest that this form of pacemaker may be useful in the case of young patients in whom cardiac arrest occurs during surgical procedures, but they stress that treatment must be immediate in such cases if it is to succeed. They recommend the use of a monitor of cardiac activity during surgical manœuvres likely to give rise to cardiac arrest, so that immediate indication would be given of this eventuality. *G. S. Crockett*

109. Auricular Fibrillation, with Special Reference to Rheumatic Heart Disease

H. R. L. Fraser and R. W. D. Turner. *British Medical Journal* [*Brit. med. J.*] **2**, 1414–1418, Dec. 10, 1955. 8 refs.

This paper from the Western General Hospital, Edinburgh, reports the authors' clinical observations on auricular fibrillation and is based on the study of 500 patients with rheumatic disease of the mitral valve. Of the 250 patients treated surgically, 42% exhibited auricular fibrillation before operation. The remaining 250 were treated medically; of 115 of these in whom the condition was mild, 4% had auricular fibrillation, while of the 135 in whom either the condition was too severe for operation or there were contraindicating complications, 80% had auricular fibrillation. Among the precipitating factors are exercise, emotion, infection, and a flare-up of the carditis, but frequently there is no obvious cause. Auricular fibrillation may cause no symptoms whatever, or on the contrary may have serious consequences, the most important of which are dyspnoea, pulmonary oedema, palpitation, anxiety, syncope, retrosternal oppression, cardiac failure, and pulmonary infarction. Also to be borne in mind is the probability of congestive heart failure in the event of pregnancy.

Although auricular fibrillation is a disadvantage in regard to operation it is not in itself a contraindication to mitral valvotomy; it had occurred preoperatively in 30% of the patients treated surgically in this series, and a further 56 (23%) developed auricular fibrillation in the immediate postoperative period. However, only 4 patients developed arrhythmia subsequently. The prognosis as regards expectation of life is less favourable than in cases of sinus rhythm. No correlation was found between auricular fibrillation and the severity of pulmonary hypertension or the degree of stenosis or of incompetence of the mitral valve. An apparent association with cardiac enlargement was found, patients with fibrillation tending to have larger hearts than those without, but the enlargement was probably only indirectly related to the arrhythmia. Myocardial damage is considered to be probably the most important factor in the pathogenesis of auricular fibrillation. Auricular fibrillation also predisposes to intracardiac thrombosis; of the 106 patients with auricular fibrillation, 43 (40%) were found to have a blood clot in the left auricle or atrium at operation, this finding being most frequent in those with severe stenosis. The presence of a regurgitant jet seemed to militate against thrombus formation. In conclusion the authors state that good operative results may be obtained in cases with auricular fibrillation, but stress that the operative risk is greater and the ultimate prognosis poorer than in cases with sinus rhythm. As stated, postoperative auricular fibrillation developed in 23% of the patients; it was found that quinidine was of little value in restoring sinus rhythm in the first 10 days, but was more successful afterwards. The prophylactic administration of quinidine was ineffective in preventing the occurrence of auricular fibrillation.

A. I. Suchett-Kaye

CORONARY DISEASE AND MYOCARDIAL INFARCTION

110. A Nutritional Program for Prolongation of Life in Coronary Atherosclerosis

L. M. Morrison. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1425–1428, Dec. 10, 1955. 19 refs.

In an investigation into the relationship between dietary fat intake and the incidence of atherosclerosis 100 patients with proved myocardial infarction have been studied at the Los Angeles County and Crenshaw Hospitals, Los Angeles, since 1946, one group of 50 having been given dietetic treatment and the remaining 50 acting as controls.

The patients were selected in that any with complications such as diabetes mellitus, hypertension, thyroid or kidney disease, and xanthomatosis were excluded; furthermore, the dietetically treated group included only patients who pledged their full cooperation and agreed to submit to continuous dietetic supervision during the years to follow. The diet prescribed contained only 20 to 25 g. of fat and about 120 g. of protein, with a total daily caloric intake of about 1,600 Cal. It was rich in vitamins, calcium, and iron, and contained a minimum of 60 g. of wheat germ and 8 g. of brewer's yeast. The daily fat intake in the control group was judged to range from 80 to 160 g. Apart from diet, the treatment of both groups was the same.

An assessment at the end of 3 years (Morrison, *Amer. Heart J.*, 1951, **42**, 538; *Abstracts of World Medicine*, 1952, **11**, 162) showed that of the 50 patients in the control group, 13 had died of cardiac failure or recurrent myocardial infarction and 2 from extracardiac causes. In contrast, of the 50 dietetically treated patients, only 6 had died of cardiac disease and one from other causes. The surviving members of the latter group had lost weight and their serum lipid levels had fallen considerably—that of cholesterol from a mean value of 312 mg. per 100 ml. to a mean of 220 mg. per 100 ml.

It is now reported that after 8 years of observation 38 of the 50 control patients had died, 22 from cardiovascular disease, whereas of the 50 dietetically treated patients, 22 had died, 9 from cardiovascular disease. (In 8 cases in the former group and in 5 in the latter the cause of death could not be determined.) The mean ages of the surviving patients in the two groups were 70 and 68 years respectively, the age range in both groups being 40 to 78 years. The mortality in the control group was comparable to the rates given by various authorities

for patients with coronary disease. No further loss of weight had occurred in the surviving dietetically treated patients.

[This is a valuable contribution to the study of dietary factors in coronary heart disease.] *Z. A. Leitner*

111. **Anticoagulant Therapy in Cardiac Infarction**

D. I. MANSON and H. W. FULLERTON. *British Medical Journal* [*Brit. med. J.*] **1**, 6–8, Jan. 7, 1956. 2 figs., 8 refs.

The authors discuss the results of treatment of cases of recent myocardial infarction at the Royal Infirmary and Woodend Hospital, Aberdeen, between 1949 and 1954. They have excluded from the survey all patients dying within 24 hours of admission, all those in whom infarction occurred more than 48 hours before admission, all those who were in hospital less than 3 weeks (unless death occurred during this period), and all patients under 40 and over 70 years old.

The remaining patients fell into three groups: (I) 102 patients (70 male, 32 female) who were given ethyl biscoumacetate for at least 3 weeks (average 4 weeks); (II) 62 patients (41 male, 21 female) who were given heparin, 12,500 units intramuscularly twice a day, for 3 weeks; and (III) 150 control subjects (91 male, 59 female) who were given no anticoagulant drugs. The dosage of ethyl biscoumacetate was controlled by estimation of the prothrombin time by the one-stage method with Russell viper venom; that of heparin was not similarly controlled. The average duration of observation in Group I was 39·5 days, Group II 33 days, and Group III 39·5 days. The results were as follows.

	Group I	Group II	Group III
No. of patients ..	102	62	150
Uncomplicated cases	79 (77·5%)	42 (67·7%)	83 (55·3%)
Thrombo-embolic complications:			
Non-fatal	15 (14·7%)	5 (8·1%)	22 (14·7%)
Fatal	6 (5·9%)	13 (21·0%)	32 (21·3%)
Total deaths	8 (7·8%)	15 (24·2%)	45 (30·0%)

Further analysis of the mortality and incidence of thrombo-embolic complications in the three decades 40–49, 50–59, and 60–69 years shows that the mortality in Group I was less than in the other groups for all decades and particularly for the decade 60–69 years. In Group II the death rate was significantly less than in Group III only for the decade 40–49 years. The incidence of thrombo-embolic complications and the death rate from this cause were again less in every decade in Group I than in the other groups. The figures for Group II, however, varied considerably from decade to decade and are therefore difficult to assess. Although the numbers are perhaps too small to allow definite conclusions to be drawn, it would appear on the whole that in this series heparin did not reduce significantly either the incidence of or the mortality from thrombo-embolic complications.

Of the 8 deaths in Group I, 6 were due to extension or recurrence of the infarction and 2 to rupture of the heart; of the 15 deaths in Group II, 11 were due to further infarction, 2 to cerebral embolism, one to cardiac failure, and one to uraemia; and of the 45 deaths in Group III, 24 were due to further infarction, 8 to thrombo-embolic complications, 8 to cardiac failure, 4 to peripheral failure, and one to an Adams–Stokes attack. Most of these deaths occurred during the first week after admission. An incomplete analysis of the deaths occurring within the first 24 hours (which were excluded from the figures considered above) also suggested that the commonest cause was a recurrence or extension of the infarction. The authors therefore suggest that heparin should be given initially in cases of myocardial infarction in addition to oral anticoagulants in an attempt to reduce the number of these early deaths. Their practice is to give 200 mg. of heparin intravenously on admission; the clotting time is then estimated at intervals of 5 hours: if it exceeds 20 minutes no more heparin is given and a further estimation is made after 2 hours; if it lies between 15 and 20 minutes 150 mg. of heparin is given; and if it is less than 15 minutes 200 mg. of heparin is given. This treatment is continued for at least 24 hours.

Arthur Willcox

112. **Metamine (Triethanolamine Trinitrate Biphosphate) in Angina Pectoris**

H. L. FULLER and L. E. KASSEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1708–1713, Dec. 31, 1955. 2 figs., 17 refs.

The action of " metamine ", the biphosphate salt of triethanolamine trinitrate, is much the same as that of glyceryl trinitrate, but its effect is both delayed and prolonged. This long-acting coronary vasodilator is well tolerated and does not give rise to undesirable side-reactions. The present authors report the results obtained with metamine in the treatment of 71 patients with coronary arterial disease; they claim that in 58 there was improvement during administration of the drug. With adequate dosage there was a reduction in the number and severity of the attacks; in some instances attacks were prevented altogether. In moderately severe cases the effective dosage was 4 mg. four times a day, but in some cases a higher dosage was necessary. The authors consider that further experimental trial of the drug is desirable. *James W. Brown*

113. **De-epicardialization: a Simple, Effective Surgical Treatment for Angina Pectoris**

D. E. HARKEN, H. BLACK, J. F. DICKSON, and H. E. WILSON. *Circulation* [*Circulation* (*N.Y.*)] **12**, 955–962, Dec., 1955. 8 figs., 32 refs.

The authors review the various methods which have been suggested for the treatment of angina pectoris by increasing the vascular supply to the myocardium and the experimental work which has been done in this connexion. They point out that the degree of success achieved with each of these methods has been remarkably constant, and conclude that increase in the intrinsic coronary flow rather than the provision of an external collateral blood supply is the most important factor, whatever the operation.

Prompted by the work of Burchell, which suggested that the epicardium is the chief barrier to vascularization of the myocardium from extrinsic sources, they have carried out experiments on dogs at the City and Peter Bent Brigham Hospitals, Boston, and Mount Auburn Hospital, Cambridge, Massachusetts, to determine the safest and most effective method of removing it. Finding that the application of 95% phenol was satisfactory in that it destroyed the epicardium without increasing the irritability of the heart, they have now applied this finding to the treatment of 18 cases of severe angina. There was no operative mortality, but 2 patients who had been relieved of pain died 2 months after operation from recurrent coronary infarction. In all but 2 of the remaining cases there was complete relief of pain. The authors consider that the results so far obtained justify the further application of this procedure for the relief of intractable anginal pain. *J. R. Belcher*

SYSTEMIC CIRCULATORY DISORDERS

114. Urologic Causes of Hypertension. 1. Hypertension Due to Renal Artery Lesions

E. F. Poutasse and H. Dustan. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **23**, 3–15, Jan., 1956. 9 figs., 88 refs.

Clinical hypertension may be primary or it may be secondary to renal, endocrine, cardiovascular, or neurogenic disorders. At one time renal hypertension was considered to be predominantly associated with pyelonephritis and obstructive uropathy; it has now been shown that hypertension can be initiated from outside the kidney by obstruction of a renal artery by embolism, thrombosis, developmental defects, aneurysm, arteriosclerotic plaques, or syphilitic arteritis. Similarly, experimental hypertension in animals can be induced by partial compression of one renal artery. This extrarenal cause of pressor substance formation produces a high blood pressure, leading sometimes to malignant hypertension, which is often cured by nephrectomy.

The changes induced in a kidney when the renal artery is obstructed, whether clinically or experimentally, are those of impaired blood supply with tubular atrophy, relative increase in fibrous tissue, and benign nephrosclerosis. Most of the renal epithelium is preserved and there are no significant changes in the arterioles. Zones of infarction may be produced as the obstruction progresses. Following these changes in the kidney the blood pressure rises and the condition may progress to fatal malignant hypertension. After death the changes in the opposite kidney are in marked contrast, being those of malignant hypertension with necrotizing arteriolar lesions.

Diagnosis is important since the prognosis after nephrectomy in cases due to obstruction of the renal artery is much better than in any other form of secondary hypertension. It is based on a history of an acute rise in blood pressure following sudden pain in one loin, and is confirmed by the presence of differences in the osmotic pressure, electrolytic concentration, and concentration of previously injected *para*-aminohippuric acid in samples of urine collected from the two kidneys by ureteric catheterization. Intravenous pyelography is of limited use; translumbar aortography shows defects in the renal artery. *W. Skyrme Rees*

115. Failure of Salt Restriction to Modify Blood Pressure in the Accelerated Phase of Primary Hypertension

G. A. Perera. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 1195–1198, Dec., 1955. 11 refs.

The effects of salt restriction were studied at the Presbyterian Hospital (Columbia University), New York, in 6 patients with malignant hypertension and advanced arteriolar nephrosclerosis who, after a control period, were given a diet containing less than 250 mg. of sodium daily for 2 weeks. No fall in blood pressure was observed (average 203/125 mm. Hg), despite a fall in the serum sodium level (average 7 mEq. per litre). In a previous study (Perera and Blood, *J. clin. Invest.*, 1947, **26**, 1109; *Abstracts of World Medicine*, 1948, **4**, 60) it was found that a similar regimen reduced the average blood pressure in 6 patients with benign hypertension from 170/109 to 152/96 mm. Hg, although there was no fall in serum sodium concentration. The present findings therefore suggest (*a*) that certain types of renal damage may introduce pressor mechanisms unrelated to sodium metabolism, or (*b*) that the distribution of sodium and water may be different in patients with extensive kidney damage from that obtaining in uncomplicated primary hypertension. *W. J. H. Butterfield*

116. Revised Concepts of the Treatment of Raynaud's Syndrome and Thromboangiitis Obliterans (Buerger's Disease)

F. L. Reichert. *American Journal of Surgery* [*Amer. J. Surg.*] **91**, 41–43, Jan., 1956. 10 refs.

The author of this paper from Stanford University School of Medicine, San Francisco, suggests that Buerger's disease and Raynaud's phenomenon are "diseases of adaptation". In 6 cases of Raynaud's phenomenon in which the acute symptoms were preceded by severe emotional upset (3 cases) or severe infection (3), treatment was aimed at restoring depleted endocrine function. The patients received tablets of desiccated adrenal cortex (dosage 3 gr. (0·2 g.) daily) and anterior pituitary body (5 gr. (0·32 g.) daily); in all cases symptoms and signs improved. In 3 cases of Buerger's disease in which this treatment was given there was apparent arrest of the condition for 3 years. A preparation of the root of *Rauwolfia serpentina* was tried on 3 patients with Buerger's disease; in 2 of these the disease was quiescent over a follow-up period of 2 years. The third patient, in whom amputation of both legs was necessary, "had no further trouble and became 'dry' after receiving rauwolfia for 4 weeks". In 33 patients with profuse sweating there was a marked decrease in perspiration after *Rauwolfia* root had been given for 2 to 4 weeks.

[Evaluation of the results in a control group receiving a placebo might be advisable.] *I. McLean Baird*

Haematology

117. **The Effects of Blood Transfusion on Renal Function.** (Функциональное состояние почек после переливания крови (Экспериментально-клиническое исследование))
N. A. Fedorov and I. I. Zaretskii. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 28–36, No. 11, Nov., 1955. 6 figs.

There have been numerous references in the literature to the important effects of blood transfusion on renal function and the role they play in the pathogenesis of post-transfusional complications. Even in cases in which no clinical reaction is evident, changes in renal function may occur. In studies on dogs the authors have estimated the glomerular function (by inulin clearance), the renal blood flow (with phenol red), and tubular reabsorption (with diodone) in order to elucidate the changes brought about by transfusions of compatible (homogeneous) blood and of incompatible (heterogeneous) blood, 10 dogs receiving 10 ml. of compatible blood per kg. body weight, and one animal 1 ml. of incompatible blood per kg., in the form of rabbit blood.

The results of these experiments were as follows. (1) For the first day or two following the transfusion of compatible blood the volume of urine and the urinary excretion of chlorides both fell; thereafter both values rose to above normal levels for a time but eventually returned to normal. (2) The glomerular filtration rate and tubular reabsorption both fell during the first 2 or 3 days, but soon returned to normal, the latter about the 6th day. (3) The renal blood flow fell for the first 24 hours, remained low, and then slowly returned to normal over the next 9 days. (4) The clearance of diodone, which measures the blood flow through the tubules, fell rapidly in the first 24 hours, then rose to normal over the next 5 days. It is thought that this finding points to the operation of factors likely to cause ischaemia of the tubules during the period immediately following blood transfusion. (5) The ratio of the urea clearance to the inulin clearance rose for the first 2 days, and then fell slowly to below the initial figure by the 6th day. (6) The filtration fraction of the plasma (that is, the glomerular filtration expressed as a percentage of the renal blood flow as a measure of the proportion of plasma which has filtered through the glomeruli) was observed to rise in the first few days after transfusion, while the glomerular filtration fell, showing that when the renal blood flow falls and so produces ischaemia of the tubules, the glomeruli on the contrary are relatively hyperaemic.

In further experiments denervation or auto-transplantation of the kidneys resulted in similar but less marked changes, but in cases in which the thalamus and hypothalamus were damaged the results obtained were exactly opposite to the above, that is, the renal blood flow and glomerular filtration actually rose in the 2 days following transfusion. It was noted that the longer the period of storage of the blood before transfusion, the more marked were the above changes. The transfusion of plasma resulted in changes analogous to those found with blood stored for a short time. It is of interest that a preliminary injection of "pantopon", given before the transfusion inhibited the changes described above, suggesting that renal function is under neurogenic control. *L. Firman-Edwards*

118. **Hodgkin's Disease. Mortality in the United States, 1921–1951; Race, Sex and Age Distributions; Comparison with Leukemia**
M. B. Shimkin. *Blood* [*Blood*] **10**, 1214–1227, Dec., 1955. 7 figs., 6 refs.

Mortality from Hodgkin's disease in the United States during the period 1921 through 1951 was analyzed with respect to race, sex and age incidence and distribution. The findings were compared with those reported for leukemia. The recorded death rate from Hodgkin's disease rose from 6·9 in 1921 to 17·0 per million in 1951. During this period, the death rate from leukemia rose from 14 to 61 per million. The death rate among males is higher than among females for both diseases; the male predominance is more marked in Hodgkin's disease than in leukemia. The rate is higher among whites than non-whites for both diseases; the white predominance is more marked in leukemia than in Hodgkin's disease. There is no peak in rate during childhood for Hodgkin's disease as there is for leukemia, and the increase in rate with age is much less steep for Hodgkin's disease than for leukemia. The mean age at death of adults dying from Hodgkin's disease and from leukemia increased by 3·5 and 8·0 years, respectively, between 1925 and 1950. The male–female sex ratio for Hodgkin's disease decreased slightly, and increased slightly for leukemia between 1925 and 1950.—[Author's summary.]

119. **Clinical Trials of *p*-(Di-2-chloroethylamino)-phenylbutyric Acid (CB 1348) in Malignant Lymphoma**
D. A. G. Galton, L. G. Israels, J. D. N. Nabarro, and M. Till. *British Medical Journal* [*Brit. med. J.*] **2**, 1172–1176, Nov. 12, 1955. 4 refs.

The water-soluble aromatic nitrogen mustard *p*-(di-2-chloroethylamino)-phenylbutyric acid (CB 1348) was tried in 62 cases of malignant lymphoma. Benefit, which is defined as improvement of real value to the patient so that he can lead something like a normal life for at least 6 months, was obtained in 4 out of 23 cases of Hodgkin's disease, 7 out of 12 of lymphocytic lymphoma, 4 out of 8 of chronic lymphocytic leukaemia, and 5 out of 6 of lymphocytic lymphoma. Improvement of shorter duration was noted in 26 other cases. Side-effects were not serious.

[The original paper should be consulted for details of the dosages administered.] *G. Calcutt*

120. Two Surveys to Investigate the Relation of Sickle-cell Trait and Malaria

H. Foy, W. Brass, R. A. Moore, G. L. Timms, A. Kondi, and T. Oluoch. *British Medical Journal* [*Brit. med. J.*] 2, 1116–1119, Nov. 5, 1955. 15 refs.

The authors report the results of an investigation carried out in Kenya into the relationship between possession of the sickle-cell trait and susceptibility to malaria. They argue that this relationship can best be studied by examining individuals rather than groups. Surveys were carried out among the Kambe and Duruma divisions of the Nyika tribe on the coast of Kenya and among the Jaluo people on the littoral of Lake Victoria, the presence of sickling in the blood being determined by incubating wet sealed preparations for 12 to 24 hours and of the malaria parasite by examining thick and thin films. Each person found to have the sickle-cell trait was paired with a non-sickling control living in the same area, the incidence of the sickle-cell trait being 33% among the Kambe, 9% among the Duruma, and 20% among one group of Jaluo and 18% among another living in a different area.

Among 326 members of the Kambe and 84 of the Duruma there was little indication of any association between the sickling and parasite rates. Among the 158 members of the first group of Jaluo the parasite rate was lower in the control subjects than in those with the sickle-cell trait, though not significantly so, while among the 324 members of the second group there was a substantially higher parasite rate in the controls. In the first group there was a higher proportion of heavy infections among the control subjects, but little general tendency for densities to be greater. In the second group 57% of the control subjects had medium or heavy infections, compared with only 33% of the sicklers.

The authors conclude that a negative association between the presence of the sickle-cell trait and malarial parasite density exists in certain areas, but that the relationship is not constant. They consider that it is unwarranted to assume that high gene frequencies for the sickle-cell trait are maintained solely by the protection afforded by the trait against malaria. *A. J. Duggan*

121. The Study of Erythropoiesis Using Tracer Quantities of Radioactive Iron

T. H. Bothwell, S. Callender, B. Mallett, and L. J. Witts. *British Journal of Haematology* [*Brit. J. Haemat.*] 2, 1–16, Jan., 1956. 2 figs., 25 refs.

122. Supplemental Folic Acid Therapy in Pernicious Anemia: The Effect on Erythropoiesis and Serum Vitamin B_{12} Concentrations in Selected Cases

A. A. Lear and W. B. Castle. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] 47, 88–97, Jan., 1956. 3 figs., 22 refs.

The effect of folic acid as a supplement to vitamin B_{12} (cyanocobalamin) as a means of stimulating haematopoiesis has been investigated at the Boston City Hospital (Harvard Medical School), Boston, in 35 patients with pernicious anaemia who had been maintained in remission on 15 μg. of cyanocobalamin monthly and who were selected for study because their haemoglobin level had been less than 12·5 g. per 100 ml. for more than one year. Intensified therapy with cyanocobalamin for 6 months resulted in an increase in the haemoglobin value in 5 of the 22 patients thus treated. An intensive course of liver extract given parenterally to 11 others was without effect. The supplemental administration of folic acid (5 mg. orally per day) during the second 6 months of the investigation produced no change in the haemoglobin level in any of the patients. Serum cyanocobalamin levels which were under 100 μg. per ml. in patients maintained on 15 μg. of the vitamin given every 4 weeks rose to over 100 μg. per ml. in all but 2 of them after intensified cyanocobalamin or liver therapy. The addition of folic acid resulted in a fall in the serum vitamin level in 18 out of 27 cases receiving the intensive vitamin therapy.

The authors conclude that folic acid deficiency is not a limiting factor in haematopoiesis, but that its administration probably increases the rate of utilization of cyanocobalamin. If, however, this vitamin is being given in suboptimal amounts to maintain full remission of pernicious anaemia the effect of the addition of folic acid may actually be deleterious. *Mary D. Smith*

123. Clinical Application of Cobalt^{60}-labeled Vitamin B_{12} Urine Test

M. I. Klayman and L. Brandborg. *New England Journal of Medicine* [*New Engl. J. Med.*] 253, 808–812, Nov. 10, 1955. 6 refs.

It was observed by Schilling (*J. Lab. clin. Med.*, 1953, 42, 860; *Abstracts of World Medicine*, 1954, 16, 42) that when vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt (^{60}Co) is administered to patients with pernicious anaemia no radioactivity can be detected in the urine unless normal gastric juice is given simultaneously. This provides the basis for a diagnostic test which the present authors have applied to a mixed group of 36 patients at the Argonne Cancer Research Hospital, Chicago. They modified Schilling's original technique by concentrating the 24-hour collection of urine by rapid evaporation to a volume less than 200 ml. and using 4-ml. samples of the concentrate for counts of radioactivity, whereas Schilling used the unconcentrated urine.

From their experience with this group of patients the authors agree that the test has clinical value, but consider that further experience must be obtained before its accuracy and limitations in clinical practice can be defined. Thus the amount of radioactivity detected in the urine of 7 patients with pernicious anaemia and of 2 who had undergone total gastrectomy was insignificant (less than 1%) in all cases; but one patient who had undergone multiple resections of the small intestine for regional enteritis and had developed megaloblastic anaemia and one with a diffuse gastric carcinoma but no evidence of pernicious anaemia also showed low excretion of ^{60}Co, although another patient with megaloblastic anaemia and 3 with gastric carcinoma showed good excretion. A third case showing low excretion of ^{60}Co remains undiagnosed. *Janet Vaughan*

Respiratory System

124. **Spontaneous Pneumothorax. A Review with the Results of Pulmonary Resection in Nineteen Patients**
J. L. EHRENHAFT, R. E. TABER, and M. S. LAWRENCE. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 801–809, Dec., 1955. 10 figs., 24 refs.

Between 1938 and 1952, 52 cases of non-tuberculous spontaneous pneumothorax, including 23 in which there was a history of recurrence, were treated at the State University of Iowa Hospitals. At the time of admission to hospital 42 of the patients had severe tension pneumothorax and 3 a severe accompanying haemothorax; in 5 the lesion was bilateral. Treatment was by needle aspiration in 7 cases, by intercostal closed drainage without suction in 12 cases, and by thoracotomy and resection of pulmonary blebs in 19 cases. [Treatment in 14 cases is not discussed.] The authors state that thoracoscopy, closed adhesion section, and sclerosing agents were not tried in this series. After resection recovery was rapid and there were no deaths or recurrences; 3 deaths occurred among the patients treated conservatively.

[The problem of multiple cysts or bullae did not arise in this series.] *S. F. Stephenson*

125. **Anaphylactic Shock from Streptokinase–Streptodornase**
W. C. SHANDS and J. H. JOHNSTON. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 320–323, March, 1956. 1 fig., 4 refs.

126. **Physiological Effects of Exsufflation with Negative Pressure (E.W.N.P.)**
G. J. BECK and L. A. SCARRONE. *Diseases of the Chest* [*Dis. Chest*] **29**, 80–95, Jan., 1956. 9 figs., 23 refs.

When spontaneous coughing is desirable but ineffective, as after abdominal operations, artificial methods of producing rapid expiratory flow rates may be applied. An apparatus for producing " exsufflation with negative pressure " (E.W.N.P.) is here described and illustrated; it causes a gradual rise of positive intrapulmonary pressure to +20 to 40 mm. Hg and then a sudden fall to −40 mm. Hg below atmospheric pressure, this rapid fall encouraging expulsion of sputum or foreign bodies. The apparatus can be used on the unconscious patient. At the Presbyterian Hospital (Columbia University), New York, the authors studied the effect of E.W.N.P. on various physiological functions in patients with bronchopulmonary disease.

In 6 healthy subjects and 6 emphysematous patients the mean heart rate was increased by 17 and 10 beats per minute respectively during E.W.N.P.; no blood-pressure change greater than 8 mm. Hg was observed, and changes in the electrical axis of the heart were no different from those produced by equivalent voluntary ventilation. In a mixed group of normal and other subjects the venous pressure during natural coughing rose by an average of 161 mm. H_2O; in 17 subjects with bronchopulmonary disease and poliomyelitis the average rise was only 58 mm. H_2O. This suggests that the rise in intrathoracic pressure produced by muscular contraction during a natural cough is higher than that needed by E.W.N.P. to produce the same rate of expiratory flow. Cardiac output, measured in one subject only, rose from 4·6 litres to 6·8 litres per minute during E.W.N.P.

The method has proved successful in the relief of dyspnoea and partial bronchial obstruction by promoting the removal of mucous and purulent plugs or blood clots, and also in the aeration of atelectatic lungs in patients with poliomyelitis, spinal-cord diseases and injuries, cerebral injuries, fractured ribs, emphysema, asthma, or bronchiectasis. After abdominal operations, the method is theoretically safer than natural coughing, since it was shown that the rise in intragastric pressure averaged only 26 mm. Hg, as compared with 85 mm. Hg during natural coughing; pain at the wound site is also less. *D. Goldman*

127. **Broncholithiasis. A Review of Twenty-seven Cases**
L. K. GROVES and D. B. EFFLER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **73**, 19–30, Jan., 1956. 6 figs., 4 refs.

128. **Detection of Early Pulmonary Emphysema**
J. K. CURTIS, H. K. RASMUSSEN, and J. T. MENDENHALL. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 569–576, Nov., 1955. 8 figs., 9 refs.

Pulmonary function tests were carried out before operation on 328 consecutive patients subjected to thoracic surgery at the Veterans Administration Hospital, Madison, Wisconsin, the object being to correlate any abnormal results with the histopathological findings in pulmonary tissue. The average age of the patients was 37 years and most of them were suffering from tuberculosis. The lungs were carefully inspected at the time of operation for the presence of emphysema. On gross examination of the resected specimens emphysema was diagnosed if blebs or bullae were found or there was destruction of alveolar walls. Of the 328 patients, 150 had significant emphysema at the time of operation or on gross examination of resected specimens.

In all the cases of emphysema vital capacity was measured; apart from a prolongation of expiration on the spirogram, no diagnostic pattern was observed. Maximum breathing capacity (M.B.C.) was determined in all 328 cases. In 92 emphysematous patients the M.B.C. was abnormal—that is, less than 95% of the predicted value, with an elevated spirogram indicating air trapping. The M.B.C. was abnormal in 22 patients

without emphysema. Of 79 patients with emphysema, in 71 the two-second timed vital capacity (T.V.C.) was 90% or less; in 18 of 34 without emphysema the T.V.C. was abnormal. There was a rise of 2% or more in the alveolar nitrogen curve after a single breath of oxygen in 59 out of 70 emphysematous patients; an abnormal nitrogen curve was also obtained in 20 out of 46 patients without emphysema. The ratio of residual air to total lung capacity was greater than 35% in 17 out of 48 cases of emphysema and in 3 out of 10 other cases. The index of intrapulmonary mixing after breathing 99·4% oxygen for 7 minutes was determined in 48 cases of emphysema, in 35 of which the index was 2·5% or greater; in 4 cases without emphysema the indices were abnormal.

Finally, in 53 cases the T.V.C., M.B.C., and alveolar nitrogen curve after a single breath of oxygen were determined; the results of all three tests were abnormal in 36 out of 43 patients with emphysema and in 3 out of 10 in whom there was no evidence of emphysema.

[The data obtained are not compared statistically.]

Denis Abelson

NEOPLASTIC DISEASES

129. The Aetiology of Respiratory Tract Cancer in the South African Bantu

P. KEEN, N. G. DE MOOR, M. P. SHAPIRO, L. COHEN, R. L. COOPER, and J. M. CAMPBELL. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 528–538, Dec., 1955. 17 refs.

During the years 1949–54 86 cases of cancer of the respiratory tract in African patients and 140 cases in European patients were referred to the Radiation Therapy Department of the Johannesburg General Hospital. These formed about 7% of all the cases of malignant disease seen in the department, both in Africans and in Europeans. The site distribution was sharply different in the two racial groups: among the Africans 54% of the primary tumours were in the nose and accessory sinuses, 14% in the nasopharynx, 15% in the larynx, and 17% in the lungs; among the Europeans the corresponding proportions were 5%, 10%, 18%, and 67%. The great majority of the primary tumours of the nose and accessory sinuses arose from the region of the maxillary antrum (39 out of the 46 African cases), while 33 out of the 40 examined histologically were squamous-celled carcinomata.

It is suggested that the preponderance of nasal tumours is attributable to the habit of taking snuff, which is common among the Bantu. The type of snuff used is a mixture of tobacco and various incinerated plants —particularly the aloe. Most of the patients with nasal cancer admitted to using more than double the amount which is reputed to be the average daily ration. The patients with these tumours mostly came from the reserves, so that it is not surprising that Higginson's survey of urban Bantus (*Cancer* (*N.Y.*), 1951, **4**, 1224) showed no specific localization of cancer in the upper respiratory tract. All the 15 Africans with lung cancer were cigarette smokers. Chemical examination of samples of snuff showed that they contained a small quantity of 3:4-benzpyrene. *Richard Doll*

130. Socioeconomic Distribution of Cancer of the Lung in New Haven

E. M. COHART. *Cancer* [*Cancer* (*N.Y.*)] **8**, 1126–1129, Nov.–Dec., 1955. 7 refs.

The methods used by the author in studying the socio-economic distribution of cancer of various sites have been described previously (*Cancer* (*N.Y.*), 1954, **7**, 455, and 1955, **8**, 34; *Abstracts of World Medicine*, 1955, **18**, 163). In the present article the incidence of cancer of the lung during the period 1935–49 in three districts of the city of New Haven, Connecticut, distinguished on socio-economic grounds as " well-to-do " (I), " middle-class " (II), and " poor " (III), is reported.

The sex and age-specific incidence for the city as a whole were similar to the pattern recorded in many other parts of the U.S.A. and in Europe. Morbidity rates standardized for sex and age, however, showed the incidence of the disease to be about 40% higher in Region III than in Region I, the ratio of observed to expected cases being 0·87 for Region I, 0·81 for Region II, and 1·20 for Region III; a similar trend was observed when the figures for men and women were taken separately. There was no evidence to suggest that the difference could be attributed to differences in completeness of reporting to the State Cancer Register or in accuracy of diagnosis. It is thought unlikely that the finding can be attributed to differences in smoking habits, and it is suggested therefore that " important environmental factors other than cigarette smoking exist that contribute to the causation of lung cancer ". *Richard Doll*

131. Lung Cancer and Tobacco Smoking in Norway

L. KREYBERG. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 495–510, Dec., 1955. 1 fig., 13 refs.

The present paper completes a series of reports emanating from the University Institute for General and Experimental Pathology, Oslo, concerning the aetiology of lung cancer as observed in Norway. The earlier conclusions were: (1) that the division of cases of lung cancer into two groups according to histological type provides a valuable basis for investigation; (2) that tumours of Group I (squamous-cell, large- and small-cell, or oat-cell cancers) have increased in frequency in recent years among men living in urban districts; (3) that the new carcinogenic situation probably consists more in changes in men's personal habits than in their working conditions; and (4) that the recorded increase in Group-II tumours (adenocarcinoma, alveolar-cell carcinoma, adenoma, and salivary-gland tumours) indicates the extent of the increase which is due to improved diagnosis.

In the present study the smoking habits of 300 patients with lung cancer were compared with those of men and women of the same age distribution, as obtained from control data collected from 4,172 men and 997 women. The comparison showed no important difference from the controls for either the men (45 patients) or women (37 patients) with Group-II tumours, but a marked difference in the habits of the men with Group-I tumours (214 patients)—the number of women with Group-I tumours (5) was too small for useful analysis. Among

the affected men there were 3 non-smokers with Group-I and 3 with Group-II tumours; hence if Group-II tumours are unrelated to smoking it is deduced that 45 of the Group-I tumours in men were also unrelated to smoking, whereas 169 (nearly 80%) were related to smoking. Belief in a connexion between Group-I tumours and smoking is strengthened by the observation that the ratio of Group-I to Group-II tumours in men increased progressively as the amount of tobacco smoked increased above 4 grammes daily—with the notable exception of men who smoked pipes only.

Detailed data are also given for the smoking habits of men with Group-I tumours according to their place of residence and type of occupation. The 3 cases of lung cancer in non-smokers occurred in countrymen employed in open-air occupations. There was no indication that the somewhat higher incidence reported previously among men in generally " dirty " occupations might be due to excessive smoking.

The author points out that the ratio of Group-I to Group-II tumours among non-smokers is lower than that reported elsewhere, partly because adenomata and the salivary-gland type of tumours are included in the Norwegian material. The very low ratio observed for women in Norway cannot be explained solely in this manner, and it is therefore suggested that men may have a special sex disposition for the development of Group-I tumours.

Richard Doll

132. **Combined Radiotherapy and Resection for Carcinoma of the Bronchus. Experiences with 66 Patients**
L. L. Bromley and L. Szur. *Lancet* [*Lancet*] **2**, 937–941, Nov. 5, 1955. 2 figs., 10 refs.

Pneumonectomy is the treatment offering the greatest hope of permanent cure for carcinoma of the bronchus, but it can be performed in only a very small proportion of cases (estimated by Smithers at about 2%). In contrast, radiotherapy is generally applicable but results in only a few 5-year survivors; it nevertheless plays an important palliative role in the relief of many of the distressing symptoms. In this paper from Hammersmith Hospital, London, the authors report the early results of a clinical trial of a method of treatment consisting in radical radiotherapy followed by resection in suitable cases. Between 1949 and 1953 732 cases of bronchial tumour from four London hospitals were assessed at a conjoint clinic and divided into eight groups according to severity and operability. The 66 cases analysed in this report belonged to the first three groups, that is, those considered respectively operable, technically operable only, and inoperable owing to the site of the growth. Initially, a tumour dose of 5,000 to 5,500 r was delivered during a 6-week course of radiotherapy. After a period of convalescence of about 4 weeks pneumonectomy was performed if further bronchoscopy showed the tumour to be operable. It was the authors' experience that irradiation had not increased the hazards of hilar dissection, and that closure of the bronchial stump with stainless steel wire was adequate.

It is of interest to note that on pathological examination of 62 of the operation specimens no tumour could be found in 29 (46·7%), and in a further 14 cases (22·5%) the tumour cells showed degenerative changes. The encouragement given to the radiotherapist by these figures will be tempered by the long-term results (as determined at the end of May, 1955) which showed that only 2 patients (out of 11 possible) survived for 5 years, 3 out of 21 possible for 4 years, 5 out of 20 possible for 3 years, and 3 out of 12 for 2 years; in 10 of the 13 survivors the tumour was a squamous carcinoma. Of the 66 cases, 14 were originally classified as inoperable, but bronchoscopy at the completion of radiotherapy revealed that regression of the tumour had occurred to such an extent that pneumonectomy had become feasible.

The most disturbing feature of the treatment adopted was the high complication rate, 18 patients (27%) developing an empyema or a broncho-pleural fistula with empyema, which proved fatal in 16. Nevertheless, although the immediate results are disappointing, the authors believe that this clinical trial has provided information to surgeons and radiotherapists which will be useful in planning new attacks upon the difficult problem of bronchial carcinoma. *R. J. M. Whittle*

133. **Primary Lymphoma of the Lung**
J. C. Cooley, J. R. McDonald, and O. T. Clagett. *Annals of Surgery* [*Ann. Surg.*] **143**, 18–28, Jan., 1956. 5 figs., 11 refs.

Commenting that authoritative evidence that primary lymphoma of the lung is a definite clinical entity was not forthcoming until the era of thoracic surgery, the authors describe 9 cases of lymphoma seen at the Mayo Clinic in 2 male and 7 female patients aged 19 to 67 years, in 8 of whom the disease seemed to have arisen primarily in the lung; in the ninth case, in a woman aged 29 with Hodgkin's disease, the evidence was less clear because the cervical and axillary lymph nodes were also involved. The clinical and radiological signs suggested either carcinoma of the bronchus or abscess of the lung; examination of the sputum and bronchoscopy were unhelpful and a definite diagnosis was only made at thoracotomy, which showed the lesion to be Hodgkin's disease in 4 cases, lymphosarcoma in 4, and reticulum-cell sarcoma in one. The lymphomatous tissue usually caused a solid infiltration of a lobe, sometimes with cavitation, but in many cases it spread across fissures into adjacent lobes, involving the bronchi; the blood vessels, however, were usually only compressed by the growth and were seriously involved only late in the disease.

Excision of the growth was possible in 6 cases; of these patients, 3 died within 3 months of operation, but 3 were alive, without signs of recurrence, 3 months, 2½ years, and 8½ years respectively after operation. Resection was impossible in 3 patients, one of whom died soon after thoracotomy, but the other 2 were alive 3½ years and 1 year 11 months respectively after operation and have been given radiotherapy. From their experience in these cases and from a study of others in the literature the authors advise early thoracotomy to confirm the diagnosis, and excision of the mass and the regional lymph nodes if this is possible, followed by prophylactic radiotherapy. *Arthur Willcox*

Otorhinolaryngology

134. Experiments on the Complete Suppression of Stammering

E. C. CHERRY, B. M. SAYERS, and P. M. MARLAND. *Nature* [*Nature* (*Lond.*)] **176**, 874–875, Nov. 5, 1955. 2 figs., 1 ref.

The authors describe two series of experiments carried out at St. Mary's and St. Thomas's Hospitals, London, which, they claim, " clearly illustrate the fact that stammering . . . is caused, not by motor, but by perceptual faults ". In the first series of experiments 25 patients (all adults) with various degrees and classes of speech difficulty were subjected to a very loud tone of about 150 c.p.s. applied through headphones and were then required to read aloud from a simple text. In 24 cases the improvement in speech was dramatic, the only exception being in the case of an individual who normally worked in surroundings with a high ambient noise-level. Both in the total duration of all hesitations and pauses during the reading of a 120-word text and in ability to make an immediate start in utterance when new starting points were indicated in the text at random and in rapid sequence a striking improvement was recorded when the tone was applied.

In the second series the patients " shadowed " (repeated concurrently) an unseen message read by an operator steadily and continuously. This " shadowing " presents no difficulties to persons with normal speech and it was found that stammerers could also be induced to " shadow " fluently when reassured, even without practice. As both fluent speech and stammering are believed to be habit-forming, the " shadowing " technique has been used in clinical treatment, with successful results in all the 5 cases of severe stammering so far treated.

T. A. Clarke

135. The Rational Approach to Immunization of the Upper Respiratory Tract

T. E. WALSH. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **62**, 569–572, Dec., 1955. 21 refs.

Writing from Washington University School of Medicine, St. Louis, the author reviews the known facts as reported in the literature concerning the common cold, now recognized to be caused by a virus or possibly several types of virus. Morbidity due to the viral infection itself is low, but it may prepare the ground for a secondary invasion of the nasal and sinus tissues, the effects of which are much more severe. Neither vaccines nor antibiotics seem to affect the viral process—which in itself is seldom important—and although antibiotics have been valuable against the secondary bacterial infection, their indiscriminate use has produced resistant strains, especially of the very organisms responsible for most upper respiratory tract infections, so that now in many sinus infections a far heavier dosage of penicillin is needed than was formerly the case. The author even goes so far as to say that " it seems not unlikely that unless infection of the respiratory tract can be prevented the necessity for surgical intervention in the treatment of complications will increase. This is already becoming evident in cases of otitis media and mastoiditis ".

In the author's view " local vaccination " is the rational approach to protection of the respiratory tissues, since on the whole the results obtained with vaccines administered parenterally have been disappointing. He has shown that when a vaccine is applied directly to the nasal mucosa of rabbits there is a concentration of antibodies in the mucosa which is far higher than can be obtained by parenteral administration, and that the animal was able to resist infection with *Pneumococcus* (which is highly virulent for the species) although there was no evidence of protective antibodies in the circulating blood. In such animals there was a marked accumulation of monocytes in the subepithelial tissue, a phenomenon which did not occur in the mucosa of animals receiving the vaccine parenterally. He therefore advises a polyvalent vaccine prepared from the common respiratory pathogens and containing a sufficient number of killed organisms; the " recommended turbidity " of the vaccine is about equal to that of 1,000 million staphylococci per c.mm. The passage of particulate matter through the epithelial barrier is known to be slow; also, as the immunity conferred by the vaccine is of short duration—probably 6 to 8 weeks—vaccine treatment should be continued through the season of respiratory infection. It is suggested also that if the pus in a sinus were removed and replaced by the vaccine the method might prove of value in the treatment of cases of chronic sinusitis.

F. W. Watkyn-Thomas

136. The Medical Treatment of Ménière's Disease

H. L. WILLIAMS. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **62**, 573–578, Dec., 1955. 17 refs.

The author discusses the literature regarding the underlying condition in Ménière's disease, in particular the valuable contribution to the pathology of the condition made by Hallpike and Cairns (*J. Laryng.*, 1938, **53**, 625) and the recent work of Weille *et al.* (*Trans. Amer. Acad. Ophthal. Otolaryng.*, 1954, **58**, 466) on the changes in the capillaries of the vascular bed of the labyrinth of guinea-pigs subjected to anaphylactic shock. He then reviews at considerable length the various methods of medical treatment which have been employed. He concludes that as Ménière's disease is a disorder which " depends on an inherited constitutional tendency to react to stress in an abnormal manner . . . too much should not be expected from medical therapy. Obviously, the tendency to react cannot be abolished by any therapy. Therefore, the expressions of the disorder may be controlled but not abolished ".

F. W. Watkyn-Thomas

Urogenital System

137. **Albuminuria in Service Recruits**
F. S. FOWWEATHER. *British Medical Journal* [*Brit. med. J.*] 2, 1419–1423, Dec. 10, 1955. 9 refs.

Tests of renal function carried out on 200 Service recruits because of the presence of albuminuria are described. After a light breakfast with only one cup of weak tea, not coffee, the bladder was emptied completely and the urine kept, 15 g. of urea in water was then given and the subject seated. One hour later the bladder was emptied, at 1½ hours a specimen of blood was taken, and at 2 hours the bladder was emptied for the third time. All three specimens of urine were examined for the presence of albumin and the volume and urea concentration of each were determined. The first specimen was centrifuged and the deposit examined microscopically. The urea concentration of the blood sample and the urea clearance were calculated.

It was found that in most instances albuminuria was abolished, or nearly so, in the sitting posture; it was regarded as benign unless the deposit was abnormal. In 6 cases in which albuminuria was believed to have followed an upper respiratory tract infection the tests were repeated: in 2 of these there was orthostatic proteinuria only, in one persistent albuminuria with a normal deposit, and in 3 an abnormal urinary deposit. There was some evidence of nephritis in 32 patients who appeared healthy on clinical examination, but no history of the condition or of an infection which might be responsible was obtained. In 4 cases, including one of gonorrhoea, the albuminuria was probably due to lower urinary tract infection. Out of 36 cases in which there was a previous history of nephritis no abnormality was found in 12 and orthostatic albuminuria only in 6. Of the 200 cases, 118 were considered to be benign, 18 to be doubtful, and 64 to show definite evidence of renal disease.

L. Capper

138. **The Diagnosis of Diffuse Nephritis in Patients with Endocarditis.** (О распознавании диффузного нефрита у больных эндокардитом)
A. K. MERZON. *Терапевтический Архив* [*Ter. Arkh.*] 27, 59–68, No. 8, 1955. 10 refs.

Among the renal disturbances which may complicate severe forms of endocarditis diffuse nephritis holds an important place on account of its effect upon prognosis. It is often difficult to diagnose, however, because in such cases it frequently presents a vague and atypical picture. None of the symptoms and signs of diffuse nephritis—oedema, haematuria, albuminuria, hypertension, azotaemia, and the presence of casts in the urine—is in itself pathognomonic, and the diagnosis must be based upon a combination of them. In the presence of endocarditis these signs are not clearly defined, and also they may occur as the result of other renal disturbances, such as infarction, venous congestion, or amyloidosis. Out of 328 cases of endocarditis investigated by the author, 95 were found to have diffuse nephritis and 48 focal nephritis, while some other type of renal disease secondary to the cardiac condition was also often present. In a number of patients in this last group many of the signs of nephritis were found at one stage or another of the illness, but disappeared with treatment of the cardiac failure. Of the patients with true diffuse nephritis only 30·5% had hypertension and 39% oedema.

The author concludes that for establishment of a diagnosis of diffuse nephritis the essential point is the persistence of the signs and symptoms of renal involvement, as determined by various laboratory investigations, in spite of changes in the patient's general and cardiac condition. It is the persistence rather than the nature and degree of the abnormalities found which will definitely confirm the presence of nephritis.

L. Firman-Edwards

139. **Glomerulonephritis in Children: a Correlation of Serial Paper Electrophoresis with the Clinical Condition**
M. REICH, D. A. COATS, and I. R. MCDONALD. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] 4, 239–249, Nov., 1955 [received March, 1956]. 2 figs., 19 refs.

At the University of Melbourne the electrophoretic pattern of the serum proteins was studied in 12 children suffering from acute glomerulonephritis (6 with and 6 without anuria) and in 3 suffering from the subacute form of the disease, the pattern being compared with that seen in 8 healthy children, one child with sulphonamide anuria, 5 children with scarlet fever, and 6 with streptococcal sore throats. Characteristic changes were observed in the children with glomerulonephritis and were shown to be related to the clinical severity of the disease. In acute glomerulonephritis the total serum protein concentration rose by about 20%. In the more severe, anuric cases this rise occurred mainly in the diuretic and early recovery phase, while in the less severe cases without anuria the rise was more gradual; with clinical improvement the total serum protein level returned to normal. The serum albumin level was low in acute glomerulonephritis, and in cases associated with anuria there was a further sharp fall in the early diuretic phase. In acute glomerulonephritis, however, the increase in the concentration of gamma-globulin above normal ranged from 70 to 450%, there being a definite correlation between the magnitude of the increase and the severity of the disease. The gamma-globulin value was highest at the beginning of clinical recovery and returned to normal more slowly than the total protein or the albumin concentration. In patients with subacute glomerulonephritis the serum albumin value was low and the α_2-globulin level was raised.

The serum electrophoretic pattern in sulphonamide anuria was normal, while the pattern in scarlet fever and streptococcal sore throat showed only slight deviation from normal.

J. E. Page

Endocrinology

THYROID GLAND

140. **Primary Myxoedema Apparently Dating from Post-partum Shock**

R. FRASER and O. GARROD. *British Medical Journal* [*Brit. med. J.*] **2**, 1484–1487, Dec. 17, 1955. 11 refs.

Hypopituitarism is one sequel of severe post-partum haemorrhage and may lead to secondary hypothyroidism. Frank myxoedema, however, is seldom a marked feature of the early stages of pituitary failure. Yet when myxoedema develops following post-partum shock it may be difficult to determine whether the thyroid failure is primary or secondary to pituitary hypofunction. The authors describe 4 cases in which symptoms and signs of myxoedema apparently dated from post-partum shock occurring 3 months to 5 years previously. Details are given of the results of laboratory investigations, which included estimation of the basal metabolic rate, the plasma cholesterol level, and the urinary excretion of 17-ketosteroids and follicle-stimulating hormone, and also water-excretion and insulin-tolerance tests; electrocardiograms were taken in all cases. In one of the patients pituitary failure was suspected on the basis of the findings. However, in all 4 patients symptoms were relieved by adequate thyroid therapy, after which the results of laboratory tests were normal.

The radioactive iodine (^{131}I) uptake of the thyroid gland before and after injection of thyroid stimulating hormone (T.S.H.) was studied in these 4 cases and, for purposes of comparison, in 25 others, the investigation including estimation of the total neck radioactivity 48 hours after administering ^{131}I, the 48-hour urinary excretion of ^{131}I, and the "T" index (Fraser *et al.*, *Quart. J. Med.*, 1953, **22**, 99; *Abstracts of World Medicine*, 1953, **14**, 232). T.S.H. was given for 5 to 9 days in the authors' cases and for 1 to 8 days in the 25 additional cases. Since in hypopituitarism the thyroid gland is often slow to respond, the authors endeavoured in the majority of cases to give T.S.H. for at least 5 days.

The results in the 29 cases are given in a table. There was no uptake of ^{131}I by the thyroid gland in the authors' 4 cases or in 12 cases of primary myxoedema. Out of 3 patients with hypopituitarism but no obvious clinical manifestations of myxoedema, 2 showed a definite and one a probable response to T.S.H.; out of 6 with hypopituitarism and definite clinical signs of myxoedema one gave a definite response, 2 gave doubtful responses, while 3, in whom hypopituitarism was of long duration, did not respond to T.S.H. In the remaining 4 patients (3 healthy controls and a "thyroid addict") there was an increase in the uptake of ^{131}I by the thyroid gland.

It is suggested that the absence of response in primary myxoedema and long-standing Simmonds's disease indicates irreversible atrophy of the thyroid gland. In such circumstances the results of ^{131}I tests alone do not permit differentiation between primary and secondary myxoedema, and pituitary function must be assessed by other means. The authors put forward three reasons for the view that in their 4 cases myxoedema was not secondary to hypopituitarism but was due to primary thyroid failure: (1) irreversible thyroid failure was present at an early stage of the illness; (2) there was no evidence of hypopituitarism after treatment with thyroid hormone alone; and (3) thyroid hormone alone corrected all manifestations of disease. *Marcel Malden*

141. **Histology of the Human Hypophysis in Thyroid Disease—Hypothyroidism, Hyperthyroidism, and Cancer**

A. B. RUSSFIELD. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **15**, 1393–1408, Nov., 1955. 6 figs., 36 refs.

Sections of the hypophysis obtained at necropsy at the Massachusetts General Hospital (Harvard Medical School), Boston, from 8 cases of thyroid deficiency, 10 cases of thyrotoxicosis, and 9 cases of thyroid carcinoma were examined after staining by the periodic-acid–Schiff reaction, with orange G as a counterstain. Six cell types are differentiated by this technique: normal basophil, acidophil, amphophil, hypertrophic amphophil, chromophobe, and hyaline basophil. The amphophil cells, which were most frequently affected in these cases, are characterized by their sparse granulation and weakly positive Schiff reaction (apart from the occasional presence of a few large granules staining intensely) and are called amphophil because they may be stained red, blue, or lavender by the Mallory method; they are identical with the thyreopriva cells, large chromophobe cells, transitional basophil cells, modified acidophil cells, and intermediate mucoid cells of other authors.

In untreated cases of thyroid deficiency the hypophysis was enlarged, with an increased proportion of amphophil and hypertrophic amphophil cells and a decreased proportion of acidophil cells. In cases which had been treated with thyroid more normal conditions obtained. In the one untreated case of thyrotoxicosis (which was associated with diabetes) the hypophysis contained an abnormally high proportion of amphophil cells, whereas the proportion was only moderately increased in cases treated with radioactive iodine or antithyroid drugs, and normal in the one case treated with potassium iodide only. The proportion of amphophil cells, and particularly of the hypertrophic ones, was increased in all cases of thyroid carcinoma, except for one which had been treated with syrup of hydriodic acid and one which had been treated with oestrogen. In most cases in which the proportion of amphophil cells was increased there was associated hyperplasia of other endocrine glands. The foetal adrenal cortex had persisted in an untreated case of infantile thyroid aplasia in a child of 13 weeks, and an increase in size of the adrenal glands was common in myxoedema and adrenal hyper-

plasia or adenomata in thyrotoxicosis. Although the urinary excretion of 17-ketosteroids had not been increased in any of the cases of thyrotoxicosis, hyaline basophil cells were usually present in the hypophysis and there were some signs of Cushing's syndrome. Other changes associated with an increased proportion of amphophil cells in some cases were ovarian stromal hyperplasia, testicular deficiency, enlargement of the pancreatic islets and symptoms of diabetes mellitus, acromegaly (in one case, with suggestive signs in another), and hyperplasia of the endometrium or mammary glands.

The findings generally support the view that the amphophil cells secrete thyrotrophin and probably also corticotrophin. Clinical evidence of an associated secretion of the two hormones is provided by the exacerbations of thyrotoxicosis which occur during stress and by the reported beneficial effect of cortisone on malignant exophthalmos and thyroiditis. The occurrence of one case of acromegaly and one of possible acromegaly among the 10 cases of thyrotoxicosis in this series and of one case of hyperostosis frontalis interna among the 9 cases of carcinoma of the thyroid may be regarded as providing supporting evidence for a common origin of the two hormones. There is also some evidence that these cells produce a gonadotrophin, amphophil-cell hyperplasia having been reported to occur in Klinefelter's syndrome, in ovarian stromal hyperplasia, and in association with a high pituitary content of gonadotrophin; the occurrence of ovarian stromal hyperplasia in most of the women in the present series (one even having large ovarian fibromata) is also suggestive.

Peter C. Williams

142. **A Quantitative Autoradiographic Study of Radioiodine Distribution and Dosage in Human Thyroid Glands**
W. K. SINCLAIR, J. D. ABBATT, H. E. A. FARRAN, E. B. HARRISS, and L. F. LAMERTON. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 36–41, Jan., 1956. 5 figs., 8 refs.

The authors describe an autoradiographic study of the variation in radiation dose to thyroid tissue after the administration of radioactive iodine (^{131}I) in various clinical conditions of the thyroid gland, as observed in some 40 patients undergoing thyroidectomy at New End Hospital, London. Before the operation a dose of 100 μc. of ^{131}I was given by mouth and measurements of the uptake of ^{131}I by the gland and of the distribution of the activity were made, generally 24 hours after administration, with a scintillation counter. After thyroidectomy the excised gland was cut longitudinally and the anterior half used for the investigation of radioactivity. Contact autoradiographs were made both of 10-μ sections and of the block from which they had been cut, and the mean and maximum blackening in each measured, the corresponding dose or activity ratios being estimated from calibration films developed simultaneously.

There was good agreement between the ratio of maximum dose to mean dose obtained from block autoradiographs and the ratio of maximum activity to mean activity obtained from section autoradiographs. In the group of patients studied the former ratio ranged from 40 to 100 (mean 70) for cases of lymphadenoid goitre, about 10 for cases of carcinoma and non-toxic nodular goitre, 7·5 for toxic nodular goitre, and 3·3 for diffuse goitre. Agreement with the histological findings in the gland was generally good. *G. B. West*

143. **The Effect of Propylthiouracil on the Biological Decay Rate of I^{131} from the Thyroid Gland in Euthyroid and Hyperthyroid Subjects.** [In English]
H. LINDERHOLM and I. WERNER. *Acta medica Scandinavica* [*Acta med. scand.*] **153**, 103–117, Dec. 20, 1955. 1 fig., bibliography.

The authors, at the University of Uppsala, Sweden, studied the effect of therapeutic doses of propylthiouracil on the rate of net loss of radioactive iodine (^{131}I), from the thyroid gland of 8 hyperthyroid and 8 euthyroid subjects.

The procedure consisted in administration of 20 to 30 μc. of ^{131}I, followed by measurement of radioactivity over the thyroid gland one hour and 48 hours later, and subsequently at intervals for 14 days. In addition the radioactivity of the urine was determined during the 48 hours following administration of the test dose. Propylthiouracil was given in a dosage of 200 mg. daily, and the measurements were repeated usually 2 to 3 weeks after the start of treatment.

In hyperthyroid patients propylthiouracil produced obvious clinical improvement accompanied by an increase in the urinary excretion and a decrease in the thyroid uptake of ^{131}I. In euthyroid patients the clinical condition was not affected, but similar changes were observed in the excretion and uptake of ^{131}I. In hyperthyroid patients the median biological half-life of ^{131}I in the thyroid gland was 30 days and propylthiouracil produced no significant change. In contrast, the median biological half-life of ^{131}I in the gland in euthyroid patients was reduced from 80 days before treatment to 24 days during the administration of propylthiouracil.

In 5 euthyroid patients with congestive heart failure the urinary excretion of ^{131}I was delayed, being relatively high 24 to 48 hours after the test dose. In the same patients the maximum uptake of ^{131}I by the thyroid gland was not attained until the fourth or fifth day; in 2 of these cases the biological half-life of the ^{131}I in the thyroid gland was exceptionally long. *Charles Rolland*

144. **Treatment of Thyrotoxicosis with Radioactive Iodine. Review of 140 Cases**
G. W. BLOMFIELD, J. C. JONES, A. G. MACGREGOR, H. MILLER, E. J. WAYNE, and R. S. WEETCH. *British Medical Journal* [*Brit. med. J.*] **2**, 1223–1229, Nov. 19, 1955. 30 refs.

Of 350 cases of thyrotoxicosis treated with radioactive iodine (^{131}I) at the Sheffield National Centre for Radiotherapy, 140 have been observed for at least a year, and in this paper the follow-up results are analysed. Generally, patients were accepted for treatment only if the expectation of life was less than 20 years—that is, less than the latent period for the development of malignant changes in the gland itself as a result of ^{131}I treatment. In practice treatment was restricted to

patients over 45 years of age, younger patients with intercurrent disease which reduced the expectation of life to less than 20 years, those who were refractory or hypersensitive to antithyroid drugs, patients experiencing a recurrence after thyroidectomy, and those with thyrotoxicosis associated with heart disease.

The dosage of ^{131}I (at first arrived at by a somewhat elaborate method of assessment and later simplified) was based on the 48-hour uptake by the thyroid gland of a tracer dose of ^{131}I and the estimated size of the gland; in most cases between 6,000 and 8,000 rads was given as a single dose. Of the 140 patients, 87 became euthyroid after a single dose, but others required two or more doses, which were given at intervals of not less than 4 to 6 months. Ultimately 118 patients were euthyroid, 17 showed evidence of hypothyroidism, and 4 were still toxic. (One patient died from a cerebrovascular condition 2 days after treatment.)

Possible complications are discussed, and it is concluded that at present there is no convincing evidence that ^{131}I treatment is likely to lead to late malignant changes in the thyroid gland. *A. C. Crooke*

145. **Response to Triiodothyronine as Index of Persistence of Disease in the Thyroid Remnant of Patients in Remission from Hyperthyroidism**

S. C. Werner. *Journal of Clinical Investigation* [*J. clin. Invest.*] 35, 57–61, Jan., 1956. 17 refs.

In normal persons or in patients with thyroid diseases other than hyperthyroidism the uptake of radioactive iodine (^{131}I) from a test dose is sharply reduced if the patient is first given thyroid or triiodothyronine. In patients with active hyperthyroidism, however, these substances have no significant effect on the uptake of ^{131}I, this lack of response providing the basis of a test for the persistence of hyperthyroid activity after treatment. At the Presbyterian Hospital, New York, the test was carried out on a group of patients who had been treated for hyperthyroidism by operation or by prolonged dosage with antithyroid drugs or with ^{131}I and who were apparently in clinical remission. A test dose of 15 μc. of ^{131}I was given and the 24-hour uptake determined. The patient was then given 75 μg. of 1-sodium triiodothyronine by mouth for 8 days, a count of residual radioactivity made, and the uptake from a second test dose of ^{131}I measured.

Most of the patients who had been treated with ^{131}I showed evidence of activity of the disease for the first 5 years after treatment, but activity then subsided progressively. In patients treated by subtotal thyroidectomy activity usually subsided within 1 or 2 years, but persisted in individual cases for much longer. In a small group of patients treated with antithyroid drugs the test results showed no consistent pattern.

The author points out that if, as seems likely, those patients in whom activity is maintained after treatment are the most liable to develop recurrent hyperthyroidism, the test should have prognostic value. Conversely, it must be remembered that an abnormal response after treatment does not necessarily indicate its failure.

M. C. G. Israëls

146. **The Action of Cortisone and ACTH on Oedematous Thyrotoxic Exophthalmos.** (Action de la cortisone et de l'ACTH sur les exophtalmies basedowiennes œdémateuses)

J. Decourt, J. M. Doumic, J. P. Michard, and J. Louchart. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] 32, 186–200, Jan. 20, 1956. 15 figs., 34 refs.

The authors describe in some detail 15 cases of thyrotoxic exophthalmos treated with cortisone or ACTH given in one or more courses of one to 4 weeks each, the daily dose of cortisone being 50 mg. and of ACTH 25 to 100 units. In the later cases the ACTH was given in a daily intravenous drip infusion over 6 to 8 hours.

In 8 cases, in 7 of which there was clear evidence of hyperthyroidism, the exophthalmos was slight; the eighth patient, a woman aged 60, who had retraction of the eyelid, palpebral oedema, and exophthalmos coming on after an emotional upset, showed no evidence of thyroid dysfunction. Two courses of ACTH, administered simultaneously with radiotherapy and iodine, had no effect.

In the remaining 7 patients (3 men and 4 women ranging in age from 21 to 48) treatment with ACTH or cortisone was started when successful treatment of the metabolic disorder with sedation, antithyroid drugs, radiotherapy, or thyroidectomy had failed to bring about improvement in the exophthalmos. There was no response in one case, but some improvement was noted in the others, though in 2 there was a recurrence of thyroid overactivity. In 3 of these cases, a man of 51 and 2 women aged 24 and 54, the exophthalmos was of moderate severity, with lid retraction and partial pareses of the extrinsic ocular muscles. In the male patient there was no evidence of hyperthyroidism, and some improvement was obtained with thyroxine. A course of ACTH produced subjective improvement but no objective change, and the patient was eventually treated by radiotherapy to the pituitary fossa. [The outcome of this treatment is not described.] In the second case a partial thyroidectomy relieved all symptoms, after medical treatment for the hyperthyroidism and administration of ACTH had failed to bring about any improvement. In the third case the exophthalmos progressed after a thyroidectomy. A course of ACTH, followed by a 4-weeks' course of cortisone, produced some improvement in the exophthalmos and palpebral oedema, but had no effect on the ocular pareses.

Finally, there were 4 cases of malignant exophthalmos, which were characteristically all in males aged 51 to 58. One of these patients showed clear evidence of hypothyroidism, but [somewhat surprisingly] thyroxine was not tried in this case. ACTH therapy led to some improvement in the palpebral oedema and ocular movements, but eventually a bilateral decompression operation proved necessary to relieve the persistent exophthalmos. The other 3 patients all had severe thyrotoxicosis. In one of these ACTH was spectacularly successful in relieving chemosis, but had little effect on the ocular protrusion. Further improvement took place after thyroidectomy. In the others, one of which ended fatally, ACTH had little or no effect.

The authors conclude that the favourable effects of ACTH, when they occur, are more marked on the oedema and ophthalmoplegia than on the protrusion of the globe. They consider that cases of recent onset are more likely to respond than those of long standing. They confirm previous observations on the lack of correlation between the severity of the hyperthyroid state and the degree of ocular involvement. The possible mode of action of ACTH is briefly discussed.

H. F. Reichenfeld

ADRENAL GLANDS

147. **Clinical Use of Fludrocortisone Acetate. Preliminary Report**

G. J. HAMWI and R. F. GOLDBERG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1598–1601, Dec. 24, 1955. 6 figs., 1 ref.

This preliminary report from Ohio State University Columbus, describes the effects of "fludrocortisone" (9-α-fluorohydrocortisone) acetate on 12 patients with various disorders.

An improvement in the mental state and a gain in weight (partly due to fluid retention) were produced in a patient suffering from anorexia nervosa. Suppression of the excretion of 17-ketosteroids and 17-hydroxysteroids was achieved in a case of adrenal virilism. Sodium retention and negative potassium, nitrogen, calcium, and phosphorus balances were observed in a 20-year-old woman with an exacerbation of chronic choroiditis; progressive improvement in the choroiditis was noted while the patient was receiving the drug.

Fludrocortisone provided satisfactory replacement therapy during and after total or subtotal adrenalectomy in 2 cases (in one of which, however, sudden hypotension following a transfusion reaction necessitated the giving of additional fluid). No increase in urinary 17-hydroxysteroids occurred after adrenalectomy, so that fludrocortisone may be given in cases of acute adrenal insufficiency without impairing the diagnostic significance of this estimation. In 6 cases of Addison's disease small doses of fludrocortisone acetate (averaging 0·5 mg. every 2 to 3 days) proved adequate for replacement purposes. Overtreatment caused rapid sodium retention and weight gain.

Denis Abelson

148. **Clinical and Metabolic Effects of Prednisone**

J. D. N. NABARRO, J. S. STEWART, and G. WALKER. *Lancet* [*Lancet*] **2**, 993–998, Nov. 12, 1955. 20 refs.

From the Middlesex Hospital, London, the authors report their experience with prednisone in the treatment of 5 cases of lymphatic leukaemia, one case of malignant lymphoma, and one of Henoch–Schönlein purpura, the dosage being one-fifth to one-third that of cortisone previously given; in a further case of Hodgkin's disease prednisone was given from the start of treatment. In order to compare the effects of cortisone, hydrocortisone, prednisone, and 9-α-fluorohydrocortisone, metabolic studies were also carried out on 2 patients receiving substitution therapy following total adrenalectomy and on one healthy male subject.

All the cases are briefly described. Clinical control of the neoplastic process with a concomitant rise in the haemoglobin level to normal or near normal was achieved for varying periods. In the first 7 cases troublesome side-effects from cortisone had become manifest; of these, only oedema and sodium retention were beneficially influenced by prednisone. The finding that prednisone had much less effect on sodium metabolism than cortisone was borne out by the results of balance studies. One patient in the series relapsed and died from a severe urinary infection some 4 weeks after beginning treatment. An initial potassium diuresis was observed in the healthy subject, in the patient with Hodgkin's disease, and in one of the patients receiving prednisone in substitution for cortisone. Creatinine output was not affected by prednisone, but the urinary excretion of nitrogen was slightly increased in those patients in whom there was potassium diuresis. In one case the results of insulin tolerance tests carried out during cortisone therapy were similar to those of similar tests performed 2 weeks after prednisone had replaced cortisone. Diabetes developed in 2 cases during administration of prednisone. The absolute eosinophil count, which was determined in the healthy subject and the 2 patients treated after adrenalectomy, indicated that prednisone was 3 to 5 times more potent than cortisone in depressing the eosinophil count.

The authors, in conclusion, emphasize that only the least serious of the complications of steroid therapy—namely, sodium retention—is prevented by the use of prednisone, and that the most serious—fulminating infections, osteoporosis, steroid diabetes, peptic ulceration, and mental changes—are just as likely to develop with prednisone as with cortisone.

H. F. Reichenfeld

DIABETES MELLITUS

149. **The Physique of Diabetics**

J. LISTER and J. M. TANNER. *Lancet* [*Lancet*] **2**, 1002–1004, Nov. 12, 1955. 1 fig., 11 refs.

In order to check a clinical impression that obese, short-limbed diabetic patients are less sensitive to insulin than those with no remarkable physical features the authors undertook a full anthropometric survey of 155 diabetics at the Royal Free Hospital, London. The patients, 40 males and 115 females, were divided into two groups according to whether the onset of the diabetes had been acute or gradual. They were then weighed, measured, photographed, and somatotyped without knowledge of the clinical group to which they belonged. Total subcutaneous fat was calculated from caliper measurements of skin-fold thickness at four different sites. Insulin sensitivity had been assessed previously in the majority of cases.

The study showed that the patients of both sexes who had had an acute onset of the disease were significantly younger, more ectomorphic, and less endomorphic than those with a gradual onset. The latter, on the other hand, had more subcutaneous fat, weighed more, and were apparently less sensitive to insulin than those with an

acute onset. The authors state that the highly endomorphic group corresponds to patients previously described as insulin-sensitive, lipoplethoric diabetics. They also suggest that a high endomorphic rating indicates an increased liability to develop diabetes, a tendency which may be held in check by limitation of the obesity associated with the endomorphy.

Charles Rolland

150. **Diabetic Amyotrophy**

H. GARLAND. *British Medical Journal* [*Brit. med. J.*] 2, 1287–1290, Nov. 26, 1955. 5 refs.

The author, writing from the General Infirmary at Leeds, describes a syndrome, observed in 12 diabetic patients, which is characterized by weakness and wasting of muscles (usually confined to the legs) with loss of tendon reflexes but without sensory changes. Pain in the affected muscles is a frequent, though not constant, feature, and in some cases the protein content of the cerebrospinal fluid is increased. This syndrome is distinguished from the well-known diabetic peripheral neuropathy with sensory changes, and is considered to be caused by the disordered glucose metabolism affecting the cord, especially in the lumbar region. The author suggests that the condition may be the presenting feature of the diabetes, and that the changes are probably always reversible by full diabetic control. *P. Hugh-Jones*

151. **Clinical Evaluation of Lente Insulin in One Hundred Nine Diabetic Patients**

E. A. HAUNZ. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 159, 1611–1618, Dec. 24, 1955. 6 figs., 15 refs.

This paper from the University of North Dakota School of Medicine records the results of a trial of "insulin lente" (insulin zinc suspension) in the treatment of 109 diabetics. (The "semilente" (amorphous) and "ultralente" (crystalline) types were not available in the United States at that time.) Patients with infections or other complications and those in whom there was considerable weight change during the trial, were excluded, but the selection was otherwise made at random from "a large diabetic practice". There were 44 males and 65 females in the series, their ages ranging from 4 to 78 years and the duration of diabetes from 6 months to 36 years. In 94 cases the patient was receiving isophane insulin and in 15 cases some other type of insulin, with varying degrees of control. Diets were kept constant throughout, the urine was tested 4 times daily, and frequent fasting and postprandial blood sugar estimations were carried out. After several weeks of "optimal control" insulin zinc suspension (I.Z.S.) was substituted for the previous type and given for periods varying from 3 to 10 months. Mixtures of I.Z.S. with unmodified insulin were tried in 12 cases.

Improved control was obtained with I.Z.S. in 31 cases, control was poorer in 6 cases, and there was no difference in the remaining 72 cases. Hypoglycaemic episodes were in some cases as severe with I.Z.S. as with other insulins. The dose of I.Z.S. needed was usually slightly smaller than that of the previous insulin. The addition of unmodified insulin appeared to be successful in enhancing the quick-acting component of I.Z.S., contrary to previous reports. The incidence of localized allergic reactions was 14% with I.Z.S. compared with 22% with other insulins; in 3 instances substitution of a special beef I.Z.S. for the original pork preparation was followed by relief of symptoms. *Denis Abelson*

152. **Fructose in the Treatment of Severe Diabetic Ketosis**

J. D. N. NABARRO, J. C. BECK, and J. M. STOWERS. *Lancet* [*Lancet*] 2, 1271–1274, Dec. 17, 1955. 3 figs., 13 refs.

Investigations were carried out at University College and the Middlesex Hospitals, London, to determine the effects and clinical usefulness of fructose in the early stages of diabetic ketosis. All the patients studied were placed on admission to hospital on a balance regimen, fluid intake being recorded and all urine collected. To facilitate comparison the balance data were corrected to a standard body surface of 1·73 sq. m. Preliminary studies, in which fructose was given by mouth without insulin to 3 untreated diabetics with moderate ketosis, indicated in one case that less than half the fructose administered was oxidized or stored, the remainder being largely converted into glucose. In the 2 other cases the rise in blood sugar level after giving fructose was as great as that occurring when glucose was given in the same dosage.

Five patients with severe ketosis were treated with insulin together with a saline–lactate solution (sodium 130 mEq. per litre, chloride 100 mEq. per litre, lactate 30 mEq. per litre), to which fructose (50 g. per litre) was added, 2 to 3 litres of the solution being administered in the first 4 to 6 hours. When the blood sugar level had fallen appreciably a solution containing glucose was substituted (composed as follows: glucose 50 g., sodium 20 mEq., potassium 30 mEq., magnesium 5 mEq., phosphate 10 mEq., and chloride 45 mEq. per litre). The mean plasma bicarbonate level in these cases was 3·9 mEq. per litre at the beginning of treatment and 17·7 mEq. per litre after 12 hours, compared with 5·0 mEq. per litre and 17·4 mEq. per litre respectively in the control group of 5 diabetics with severe ketosis who were given the saline–lactate solution without fructose. Ketosis cleared rapidly in both groups. There was no proportionate increase in glycosuria in those cases in which fructose was added, but the dose of insulin given was greater than in the control group. The reduction in plasma potassium level was no greater in the former, suggesting that the larger amount of hexose retained was not stored. Some difficulty was encountered in judging the dose of insulin required owing to the fact that the blood sugar determined by the usual methods includes both glucose and fructose. Thus one of the patients had a hypoglycaemic attack when the total blood sugar level was 130 mg. per 100 ml., of which it was later found that only 50 mg. was glucose.

It was concluded that no advantage is to be gained from the early administration of fructose in severe diabetic ketosis. *Denis Abelson*

The Rheumatic Diseases

ACUTE RHEUMATISM

153. Capillary Microscopy in Rheumatic Fever

E. DAVIS and J. LANDAU. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 51–56, Jan., 1956. 3 figs., 12 refs.

This paper reports the findings on examination of the capillary patterns in the conjunctiva and nailbed in 100 patients with rheumatic fever or rheumatic heart disease at the Rothschild Hadassah University Hospital, Jerusalem. This group included both active and inactive cases. Similar examinations were carried out on a control group of 158 " nonrheumatic patients " [which nevertheless included 30 cases of rheumatoid arthritis and 11 of collagen diseases].

A characteristic capillary pattern was found in the conjunctiva in 79 and in the nailbed in 31 of the 100 rheumatic patients, the corresponding figures for the control group being 11 and 7. The special feature seen in the conjunctiva was the repeated subdivision of vessels and the abrupt thinning of the end capillaries, which was in marked contrast to the usual picture of an interlacing latticework of conjunctival vessels. In the nailbed several capillaries would often branch out from a common stem. Analysis did not show any correlation of these capillary patterns with sex, age, or the activity or chronicity of the rheumatic process.

A higher incidence of these changes was found among 26 non-rheumatic members of 22 families in which there were 32 cases of rheumatic fever or rheumatic heart disease than among controls. It is therefore thought possible that the patterns may be present before the onset of rheumatism and may be associated with a rheumatic diathesis rather than with the disease itself. The presence of these capillary signs may help in the diagnosis of borderline cases. *G. W. Csonka*

154. Prevention of Rheumatic Fever by Treatment of Previous Streptococcic Infections

A. J. MORRIS, R. CHAMOVITZ, F. J. CATANZARO, and C. H. RAMMELKAMP. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 114–116, Jan. 14, 1956. 7 refs.

Although it has been shown that adequate treatment of streptococcal infections with penicillin will prevent the subsequent development of rheumatic fever, it has never been clearly determined whether sulphonamides, which are still widely used for the treatment of streptococcal pharyngitis, have a similar protective effect. At a U.S. Air Force base a total of 291 patients with pharyngitis were treated with 2 g. of sulphadiazine followed by 1 g. every 6 hours for 5 days. Group-A haemolytic streptococci were isolated from the oropharynx of 261 patients, who were then compared with 264 similar patients who received no specific treatment. After 9 days 66% of the treated group and 88% of the control group still harboured the organism; the figures at the end of 13 days were 82% and 85% respectively. A relapse occurred in 21 (8%) of the treated patients compared with 7 (2·7%) of the controls. Suppurative complications (peritonsillar cellulitis, otitis media, or sinusitis) developed in 11 (4·2%) of the patients receiving sulphadiazine and in 17 (6·5%) of the control group. The reduction in the incidence of these complications in the treated group was confined to the first week, the incidence during the second week being the same in both groups. Of the treated patients, 14 (5·4%) subsequently developed rheumatic fever and a further 6 mild symptoms suggestive of rheumatic fever. Rheumatic fever occurred in 11 (4·2%) of the control subjects.

It is concluded that sulphadiazine in the dosage used does not eradicate the infecting organism or prevent the development of rheumatic fever, although it reduces the incidence of suppurative complications while it is being given. The higher relapse rate after the treatment of streptococcal pharyngitis with sulphadiazine is presumably due to inhibition of the organism delaying the development of immunity to it.

[These findings do not of course in any way invalidate the use of sulphonamides in the *prophylaxis* of haemolytic streptococcal pharyngitis and of rheumatic relapses.]

C. Bruce Perry

155. Observations on the Electrocardiographic Changes in Acute Rheumatism

R. FIFE and W. R. MURDOCH. *Glasgow Medical Journal* [*Glasg. med. J.*] **36**, 379–392, Nov., 1955. 1 fig., 37 refs.

A review is presented of the electrocardiographic changes found in 62 cases of acute rheumatic carditis in patients aged 4 to 40 years who were admitted to Law Hospital, Carlisle, within 6 weeks of the onset of the attack.

Auricular fibrillation was present in 3 cases. The P–R interval was prolonged in 7 (11%). Deviation of the S–T interval occurred in 16 cases, but 6 of the 8 patients in whom it was elevated had pericarditis, while in 3 of those in whom it was depressed ventricular hypertrophy was also present.

The presence of negative T waves in Leads V1 to V4 is normal in children, but in 10 cases of the present series it was accepted as evidence of carditis as subsequent records showed a lessening of the negativity. In 4 cases the changes were slight.

The existence of several different standards of normality for the Q–T interval makes the significance of small increases difficult to assess; according to one standard the interval was prolonged in 27 of the cases, and according to another standard in only 3.

The authors are of the opinion that changes in the S–T segment and the T wave are of more value in the

diagnosis of carditis in acute rheumatism than an increase in the Q–T interval and they stress the importance of serial tracings. They suggest that no definite conclusion as to the prognostic value of electrocardiographic findings in rheumatic carditis is justified in the present state of knowledge.

[It is evident that though electrocardiographic changes occur in a proportion of patients with rheumatic carditis, the diagnosis must usually be made on other grounds.]

C. W. C. Bain

156. **Early Diagnosis and Treatment of Rheumatic Coronary Arteritis.** (Ранняя диагностика и лечение ревматических коронаритов)

G. M. Efimova. *Советская Медицина* [*Sovetsk. Med.*] 40–46, No. 12, Dec., 1955. 3 figs.

After a brief review of the Russian literature on the subject of coronary involvement and cardiac infarction during the acute stage of rheumatic fever, the author reports, from the Sverdlovsk Medical Institute, her own series of 30 cases of " rheumatic coronaritis " in adults. On the basis of the clinical and electrocardiographic (ECG) findings the patients were divided into two categories: (1) the " infarction " group (4 cases), and (2) the " stenocardiac " (coronary insufficiency) group (26 cases). The symptoms and signs in patients in Group 1 were severe precordial pain, tachycardia, moderate fever, leucocytosis, increase in the erythrocyte sedimentation rate, and deep inversion of the T wave in the ECG. Symptoms in the patients in Group 2 were less severe, and the ECG showed in some cases inversion of the T wave and in others a high or low S–T take-off.

Treatment with salicylates and amidopyrine is recommended, combined with strict bed rest for a period of 6 weeks for patients in the first group and of 2 to 3 weeks for those in the second.

[The electrocardiograms reproduced represent only four leads, namely, I, II, III, and CR4, and are not convincing.]

A. Swan

157. **Estimation of Adrenocortical Hormones in Patients with Rheumatic Carditis Undergoing Treatment.** (Исследование гормонов коры надпочечников у больных с кардиальной формой ревматизма в связи с гормональной терапией)

E. A. Toloknova. *Терапевтический Архив* [*Ter. Arkh.*] 27, 68–73, No. 8, 1955. 5 figs.

Serial estimations of adrenocortical hormones were made on a group of 42 patients with rheumatic carditis, of whom 25 were treated with ACTH, 11 with " butadion ", and 6 with salicylates. The serum 11-oxysteroid level was estimated by the method of Cornelius and MacDonald (as modified by Bush), while urinary 17-ketosteroid excretion was determined by Zimmerman's method as modified by Preobrazhenskii.

The findings may be summarized as follows. (1) The urinary content of 17-ketosteroids is lowered in most cases of rheumatic carditis. (2) The serum 11-oxysteroid level may be lowered, normal, or even raised during certain forms of treatment. (3) ACTH causes a sharp rise in the serum level of these hormones, but this tends to fall after the cessation of treatment. (4) Butadion causes similar but less marked changes. (5) Salicylates cause a slight rise in the urinary excretion of 17-ketosteroids.

In many of the cases in all three groups the blood 11-oxysteroid level and the urinary excretion of 17-ketosteroids before treatment were lower than the average for the control subjects.

L. Firman-Edwards

CHRONIC RHEUMATISM

158. **Swellings in the Region of the Second and Third Metacarpophalangeal Joints with Lesions of the Cervical Nerve-roots.** (Über Schwellungen in der Umgebung des zweiten und dritten Fingergrundgelenkes bei zervikalen radikulären Reizzuständen)

W. Gensler. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **14**, 282–291, Oct., 1955. 3 figs., 26 refs.

Among 30,000 patients examined at a Hamburg rheumatism clinic during a period of 18 months swellings confined to the second and third metacarpo-phalangeal joints were observed in 102 cases, being bilateral in 43. There was thickening of the skin and of the underlying fatty tissue, but no sign of arthritis and no bone changes demonstrable by *x* rays. Pain in the arms and paraesthesiae were common, together with tenderness and limitation of movement of the cervical spine and tenderness in the region of the brachial plexus and of the muscles of the upper arm. There was some weakness of adduction of the fifth finger. Chronic " septic foci " were found in 84 cases. Radiographs of the cervical spine showed degenerative changes and narrowing of the intervertebral foramina. It is suggested that this type of swelling results from a reflex irritation of the spinal roots and must be differentiated from rheumatoid arthritis.

John Lorber

159. **Serum Globulin Fractions in Chronic Rheumatic Diseases**

H. B. Salt. *Clinical Chemistry* [*Clin. Chem.*] **2**, 35–44, Feb., 1956. 18 refs.

Microelectrophoretic separation of the serum globulins was carried out at the Worcester Royal Infirmary in 27 cases of subacute and chronic rheumatic disorders of various types. Those cases in which the serum globulin level was within normal limits (below 3·7 g. per 100 ml.) were separated from those with hyperglobulinaemia and a more detailed study made of the abnormal globulin patterns in the latter group (14 cases). The possibility of assay of γ globulin by a simple salting-out method was also explored.

Statistical analysis showed that there was a significant difference between the two groups in respect of each and every protein fraction. Where the serum globulin level was normal the total protein and albumin levels were also substantially normal, as was that of each globulin fraction. In the hyperglobulinaemic group the total protein level was increased and the albumin level

reduced in most cases. The hyperglobulinaemia was most frequently due to an increase in the γ-globulin fraction, often accompanied by an increase in the α_2-globulin fraction. Where electrophoretic analysis showed the serum γ-globulin level to be within normal limits the figures were in close agreement with those obtained by a salting-out method in which an ammonium-sulphate–sodium-chloride reagent was used; but where the serum γ-globulin level as determined by electrophoresis was increased the salting-out technique gave results which were significantly lower. That this may have been due to heterogeneity of the proteins was suggested by the presence of split peaks in the electrophoretic patterns.

[No reference is made to the relationship between these changes and the clinical type of rheumatic disorder or the duration or phase of the rheumatic process—factors to which other authors have ascribed an influence on the levels of the individual globulin elements. The salting-out process is not related to other, more usual, chemical methods of estimating γ globulins.] *Harry Coke*

160. **Use of Reserpine in Psychogenic Rheumatism, Osteoarthritis, and Rheumatoid Arthritis. A Preliminary Report**

H. BARTFELD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **159**, 1510–1513, Dec. 17, 1955. 7 refs.

The action of reserpine in 7 cases of psychogenic rheumatism, 16 of osteoarthritis, 4 of rheumatoid arthritis, and 3 of mixed osteoarthritis and rheumatoid arthritis was observed at New York University Post-Graduate Medical School. The drug was given in a dosage of 0·1 mg. twice daily, increased to 0·25 mg. twice daily in some cases if there was no response. Of the patients with psychogenic rheumatism, 5 derived benefit—usually less stiffness and muscle pain—from the treatment [but only 2 are mentioned in any detail]. Of the remaining 23 patients, 9 showed some temporary symptomatic improvement. [Objective changes are not mentioned.]

The author concludes that reserpine may help to relieve symptoms in rheumatic disorders and that it should be combined with routine treatment.

K. C. Robinson

161. **The Spondylitis of Juvenile Rheumatoid Arthritis**

R. E. BARKIN, J. S. STILLMAN, and T. A. POTTER. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 1107–1110, Dec. 22, 1955. 8 figs.

Spinal involvement in juvenile rheumatoid arthritis has occasionally been noted in the literature, but has never been adequately investigated. The present authors have therefore undertaken a survey of all the cases of Still's disease seen over the last 40 years at the Robert Breck Brigham Hospital, Boston, which is largely devoted to rheumatic diseases, in order to determine the incidence and nature of the spondylitis. Clinical or *x*-ray evidence of spinal involvement was found in 57 (80%) of 71 cases, the areas most commonly affected being the neck and lower back. Calcification of the paravertebral ligaments was, however, unusual, being noted in only 2 cases in this series. The symptoms of spinal involvement generally appeared at, or soon after, the onset of the illness, and one of the ultimate results was a shortening of stature owing to interference with the normal growth of the spine. In no case was spinal arthritis present in the absence of peripheral joint involvement.

In the entire series there were 45 female children and 26 male, in general a similar distribution to that commonly seen in rheumatoid arthritis in adults. Of the 57 patients with evidence of spinal involvement, 37 were female and 20 male—a distribution differing significantly from that of spondylitis in adults. This suggests that the disease is part of the process of juvenile rheumatoid arthritis and not a true spondylitis *sui generis* as in most adults. *W. S. C. Copeman*

162. **Involvement of the Kidneys in Rheumatoid Arthritis.** (К вопросу о поражении почек при так называемом неспецифическом инфекционном (ревматоидном) артрите)

V. V. SURA and I. I. MAKARENKO. *Советская Медицина* [*Sovetsk. Med.*] 46–50, No. 12, Dec., 1955.

Analysis of the urine in a group of patients with rheumatoid arthritis at the Lenin Institute of Hygiene, Moscow, showed that 26 had some degree of renal involvement. In 16 of these cases no other condition was found to account for the urinary changes and the renal lesion was consequently attributed to the rheumatoid arthritis. In 3 of the cases there was severe albuminuria, with casts, leucocytes, and a few erythrocytes in the urine; in the remainder, however, the albuminuria was slight, and casts and blood cells were scanty. In all 16 cases treatment with ACTH and cortisone completely cleared up or greatly improved the rheumatic manifestations but had no influence on the urinary findings or, the authors therefore conclude, on the renal lesion. *A. Swan*

163. **The Presence of Natural Hydrocortisone in Synovial Fluid**

C. L. COPE and C. E. SEWELL. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 392–396, Dec., 1955. 13 refs.

In a study carried out at the Postgraduate Medical School of London the authors have estimated the hydrocortisone content of synovial fluid removed from the knee-joints of patients with rheumatoid arthritis or similar conditions. The method of extraction of hydrocortisone from the joint fluid is described in detail. Paper chromatograms of a solution of the extract were then prepared, a parallel chromatogram being run with a standard sample of authentic hydrocortisone (free alcohol). When dry the chromatogram was examined under ultraviolet light and the opaque hydrocortisone spots outlined in pencil. The chromatogram was then developed by dipping it in a blue tetrazolium reagent, which produces bluish-violet zones on the paper where it is reduced by steroids such as hydrocortisone. The hydrocortisone was recognized by (1) its reduction of the tetrazolium reagent, (2) its opacity to ultraviolet light,

and (3) identification of its rate of flow on the chromatogram with that of the authentic hydrocortisone. After elution of the spots the hydrocortisone content of the synovial fluid was then determined in a colorimeter, comparison being made with the pigment from the authentic hydrocortisone spot.

The mean concentration of hydrocortisone in 13 samples of synovial fluid was $6{\cdot}8 \pm 3{\cdot}6$ μg. per 100 ml. The mean value in 9 samples from patients receiving oral cortisone was $8{\cdot}7 \pm 2{\cdot}7$ μg. per 100 ml.; the difference between these two results is not significant. The mean concentration of the steroid in synovial fluid was similar to the mean concentration in the blood. The authors therefore conclude that difficulty of access of natural hydrocortisone to the joint cavity is not an important aetiological factor in rheumatoid arthritis.

C. E. Quin

164. **Experience with Cortisone in the Management of Rheumatoid Arthritis**

COMMITTEE OF THE AMERICAN RHEUMATISM ASSOCIATION. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 325–336, Dec., 1955. 3 refs.

The results are reported of a study sponsored by the American Rheumatism Association of the experience of certain clinics in the treatment of rheumatoid arthritis with cortisone. The objectives of the study were to determine how best to plan a controlled comparison of the effects of various treatments, to seek any possible correlation between variations in the response to treatment and particular features of the disease or mode of treatment, and to look for any explanation of the differences between the reports of different centres concerning the efficacy of treatment. Altogether, 546 patients were treated with cortisone at 13 clinics, uniform criteria for inclusion being adopted, and data were collected by means of a comprehensive questionary to be completed by the participating clinic in each case. Information was obtained concerning the progress and stage of the disease, previous treatment, concomitant disease, occurrence of undesirable effects of cortisone, and response to the drug. Of the 546 patients, 37% were males and 63% females; there were 3 patients under 5 years and 4 over 80 years of age, but the majority were between 35 and 60. The dosage of cortisone was less than 50 mg. a day in 43% and more than 50 mg. in the remainder.

The data are analysed in detail, but wide variations made it difficult to achieve their declared objectives. Thus the proportion of favourable results reported from different clinics varied from *nil* to 70% and that of unfavourable results from 22 to 93%. The authors ascribe these differences to variations in the judgment of the participating physicians rather than to variations in the reactions of the patients. Major side-effects were reported in 46% and minor side-effects in 72% of those treated. The major occurrences included pathological fractures, with an incidence of 0·6% in patients aged 30 to 44 rising to 9·8% in patients over 60, and peptic ulcer, with an incidence ranging from 9·3% in patients of 20 to 44 to 2% in patients over 64 years.

The authors discuss the merits and defects of a study of this kind and consider how the difficulties revealed can be overcome in planning future large-scale investigations of the effects of various remedies in the treatment of rheumatoid arthritis. *William Hughes*

165. **Rehabilitation of the Rheumatoid Arthritic Cripple**

E. W. LOWMAN. *Journal of the South Carolina Medical Association* [*J. S. C. med. Ass.*] **51**, 421–426, Dec., 1955.

A combination of medical treatment, rehabilitation, and vocational guidance was given to two groups of patients with active rheumatoid arthritis at the Goldwater Memorial Hospital, New York. Group I contained 24 severely disabled patients, while Group II contained 26 who were less badly disabled but were unable to continue their occupation; later, 6 patients had to be dropped from each group. Steroid therapy was necessary to control the arthritic process in 25 of the 38 patients and phenylbutazone in 8; only 5 could be maintained on salicylates alone.

In Group I medical treatment reduced the average "functional deficiency" from −60% to −53%; after intensive rehabilitation functional deficiency was −29%, the average duration of treatment being 339 days. One patient was placed in suitable occupation and 13 were discharged wholly or partly self-sufficient; 4 patients had to remain in hospital. In Group II medical treatment reduced the average functional deficiency from −30% to −13%; after rehabilitation the figure was −4%, the average duration of treatment being 223 days. All the patients in this group were discharged wholly or partly self-sufficient, 7 being placed in suitable work.

The author has found that among the more important factors which help in the selection of patients suitable for rehabilitation are adequate medicinal control of the arthritic process, reasonable mechanical integrity of the joints, and a good psychological outlook on the part of the patient. Other factors which influence selection are the applicability or otherwise of self-help devices and the socio-economic resources of the patient.

B. E. W. Mace

166. **Serum Proteins, Glucoproteins, and Lipids in the Various Clinical Forms of Ankylosing Spondylitis.** (Protides, glucides et lipides sériques dans les diverses formes cliniques de la spondylarthrite ankylosante)

F. JACQUELINE and J. GROULADE. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 735–744, Nov., 1955. 3 figs., 25 refs.

At the Centre for Research in the Rheumatic Diseases, Aix-les-Bains, the authors have studied the serum protein content and pattern in 54 cases of ankylosing spondylitis and in 32 normal male control subjects, other cases of ankylosing spondylitis with associated diseases likely to produce changes in the serum proteins being excluded. Zone electrophoresis on paper was followed by staining with naphthalene black for protein, periodic-acid–Schiff stain for glycoprotein, and Sudan black for lipid. In addition, an estimate of the total serum glyco- and lipoprotein content was made by staining the serum on paper without electrophoresis and comparing it with a standard

pooled serum from a group of healthy blood donors aged between 30 and 40. The cases were divided into two groups—those with and those without peripheral joint involvement. The patients showing only spinal disease were further divided into (1) those in whom the process was relatively painless, the course slow, and radiography showed intervertebral bony bridges and no osteoporosis; and (2) those with more painful and disabling disease, with early apophyseal joint fusion, much vertebral rarefaction, and little bridging.

Purely spinal cases without osteoporosis showed a slightly, in some cases a considerably, increased serum albumin content, in contrast to hypoalbuminaemia in the other cases. The level of the α_2 globulins, and especially that of the associated glycoproteins, was elevated, the glycoprotein level corresponding with the activity of the disease process. The authors consider that in this group the serum glycoprotein content gives a better indication of activity than does the erythrocyte sedimentation rate or the severity of symptoms. Cases with spinal osteoporosis invariably showed a considerable lowering of the serum albumin content and a persistent elevation of that of α_2 globulin and glycoprotein. The patients with peripheral joint involvement had a lowered serum albumin and a raised α_2-globulin content and a greater increase in γ globulin than in the preceding groups. The increase in the total and α_2-glycoprotein levels and the erythrocyte sedimentation rate paralleled the degree of clinical activity of the disease. The serum lipid content showed little change throughout, apart from that which would be expected to result from age.

S. C. Milazzo

167. **Osteoarthritis of the Cervical Spine. Stage and Treatment**

J. G. KUHNS. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 60–64, Jan. 12, 1956. 4 figs., 14 refs.

Osteoarthritis of the cervical spine is a progressive disorder—in most cases slowly progressive—in which, clinically, there are three stages. In the early stage, in which the radiological changes are slight, the symptoms are pain and stiffness and spasm in the antigravity muscles of the neck; in the second stage, in which the radiograph shows narrowing of the intervertebral spaces, the chief symptom is pain referred to the dermatomes of the nerve roots that are irritated; in the third stage there are advanced radiological changes with severe limitation of movement, deformity in the cervical region, and local and root pain. Symptoms in the early stage are most effectively treated by temporary application of a padded collar; this should be worn until symptoms subside, but should be removed several times a day for local heat treatment. Endocrine disturbances should be corrected and foci of infection removed. The aim of treatment in the second stage is directed to relief of pressure on the nerves, for which a firm bed without pillows or at most a small pillow under the nape of the neck is advised. Heat treatment is also given. In most cases relief follows the almost continuous application of traction of 5 to 10 lb. (2·2 to 4·5 kg.) to the cervical spine with the patient supine on a firm bed. If no improvement in root pain follows traction for 2 weeks the pressure on the nerve must be relieved surgically. In the third stage traction may give temporary relief, but the most effective treatment is application of a firm collar, fitting well over the shoulders and supporting the occiput and chin; this can be made of plastic material from a plaster model. In these cases medical supervision must continue for the remainder of the patient's life.

Kenneth Stone

168. **Osteo-arthritis. An Approach to Surgical Treatment**

J. TRUETA. *Lancet* [*Lancet*] **1**, 585–589, May 5, 1956. 13 figs., 14 refs.

169. **Changes in the Corium and Subcutaneous Tissues as a Cause of Rheumatic Pain**

D. M. BAKER. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **14**, 385–391, Dec., 1955. 6 figs., 9 refs.

In continuation of her previous studies (*Lancet*, 1951, **2**, 753; *Abstracts of World Medicine*, 1952, **11**, 80) the author presents further observations on the syndrome usually known as panniculitis, in which there is a rapid increase in weight, often at the time of the menopause, and the patient complains of heaviness and aching in the affected parts, these symptoms being increased by exercise and by warmth. Two main signs are described: (1) the skin appears to be "tacked down" over the affected part so that it is impossible to lift it away from the underlying tissue, and mottling or an appearance of *peau d'orange* is produced when the skin texture is tested by palpation; (2) the skin over the affected area feels dense, almost indurated, and shows a lack of elasticity. These signs are best elicited in the skin in front of the external auditory meatus.

Examination of skin biopsy material from 49 patients suffering from this syndrome, and of skin from unaffected areas of the patient's body or from normal adults as control specimens, showed that in 40 cases (80%) there was an apparent increase in depth of the collagen layer of the dermis, the collagen appearing in some sections to dip down into the fatty tissue; the collagen fibres were mature and acellular. No abnormality was seen in the fat. Electron microscopical examination of the collagen tissue showed that the period of the striations of the collagen fibrils and the diameter of the individual fibrils were no different from those of normal skin. The pathological findings are correlated with the symptoms and signs, and the treatment is discussed. It is pointed out that the most important part of treatment is to produce a gradual but steady reduction in the patient's weight. Heat treatment is not advisable as it tends to increase the pain, but mild general exercises are usually beneficial and massage sometimes of value. The administration of phenylbutazone, 0·4 g. daily, and of cortisone, 75 mg. daily, appears to give some relief of symptoms, provided that they do not cause water retention. It is believed that in most cases the condition is eventually self-limiting. The author suggests that panniculosis would be a better name than the misleading term panniculitis.

C. E. Quin

Physical Medicine

170. **The Ineffectiveness of Splinting in the Treatment of Abductor Paralysis at the Shoulder**
W. J. W. SHARRARD and J. KNOWELDEN. *Lancet* [*Lancet*] 1, 9–13, Jan. 7, 1956. 2 figs., 9 refs.

In a closely argued and well-documented paper the authors question the wisdom of the time-honoured practice of applying an abduction splint in cases of paralysis of the shoulder muscles, and particularly of the deltoid muscle.

An analysis of 359 cases of abductor paralysis in the upper limb from acute poliomyelitis showed that splinting in abduction diminished the recovery of the paralysed deltoid muscle and was of no benefit when the muscle was paretic. Moreover, increased laxity of the shoulder-joint resulted from splinting, while scoliosis was never seen as a result of failure to maintain abduction in cases in which the muscles of the upper limb alone were affected. On the other hand immobilization of the limb by the side in the acute stage of the disease, as is necessary for respirator treatment, produced severe adduction contracture which was avoided in the unsplinted limb by daily passive movement. It is concluded that except in the acute stage and in special circumstances in the convalescent stage of poliomyelitis, splinting of the arm in abduction " is unnecessary and sometimes harmful ".

[The authors' argument is well worth studying in the original. One conclusion only, that concerning scoliosis, appears to the abstracter to be less soundly based than the others, as no mention is made of the important part played in causing this deformity by the latissimus dorsi muscle, which is innervated by the same segments as are the shoulder muscles.] *L. Michaelis*

171. **Vertebral Manipulation.** (Les manipulations vertébrales)
S. DE SÈZE and J. THIERRY-MIEG. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 633–650, Sept.–Oct., 1955. 10 figs., 5 refs.

Although manipulation of the vertebrae has long been practised by osteopaths, it was only about 1944 in France that scientific appraisal of this method of treatment showed that it had a part to play in orthodox medical treatment. In this paper the authors describe the methods adopted at the Hôpital Lariboisière, Paris. They first consider the pathological anatomical changes which in their view are responsible for acute and chronic lumbago and for sciatica, and go on to describe in detail the manipulations necessary to relieve these conditions. They then suggest possible ways in which manipulation can correct the pathological processes affecting the intervertebral disk.

The authors consider that acute lumbago is the lesion most amenable to this form of treatment, as here the pathological condition is reversible, although they add that no guarantee can be given that relapse will not occur. In the treatment of sciatica, however, success was achieved in only 40% of their cases, largely, they suggest, because in many of these the pathological process had become irreversible; this was the case also in chronic lumbago, in which the results of manipulation were not so uniformly good as in acute lumbago. They state that difficulties arising from this type of treatment are few, provided that the manipulator is expert and that no mistake has been made in diagnosis. In their view vertebral manipulation should not be regarded as a specialty, but rather as a part of physical medicine as a whole. *W. Tegner*

172. **The Treatment of Lumbago and Sciatica by Vertebral Manipulation.** (A propos du traitement des lombalgies et sciatiques par les manipulations vertébrales)
J. A. LIÈVRE. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 651–656, Sept.–Oct., 1955.

The author discusses critically the results achieved by vertebral manipulation in the treatment of lumbago and sciatica. He agrees that in certain cases this form of treatment is successful, either immediately or gradually after a prolonged course, but points out that it should not be forgotten with regard to the latter type of case that spontaneous remissions occur in both sciatica and lumbago, and also that the development of strong psychological influences between patient and manipulator play their part in helping the patient. He also emphasizes that not all manipulations are successful—in some cases the condition persists in spite of the treatment, and in some even gets worse, and cases of paraplegia, fortunately few, have occurred.

Analysing reports on the success of manipulation, which he does with caution and reserve, the author concludes that this form of treatment is interesting and occasionally sensational, but often only of little value, and on no account should other methods of treatment be abandoned. He considers that the inflammatory factor as well as the purely mechanical one must be borne in mind in considering the aetiology of lumbago and sciatica. His perusal of some American works on chiropractic and osteopathy has convinced him that the views on aetiology expressed therein are infantile. Hitherto these methods have been largely in the hands of non-medical practitioners many of whom perform manipulation with great vigour, whereas in fact it should be carried out with the greatest gentleness, and never under a general anaesthetic. The practitioner must be an experienced diagnostician, and should accept only those cases referred to him for manipulation which are suitable for this treatment, for each case must be judged on its merits. The author stresses that manipulation must be a medical technique, and that physiotherapists should be instructed and controlled by medical men. *W. Tegner*

Neurology and Neurosurgery

173. **The Electroencephalogram in Retrolental Fibroplasia**

E. L. GIBBS, A. FOIS, and F. A. GIBBS. *New England Journal of Medicine* [*New Engl. J. Med.*] **253**, 1102–1106, Dec. 22, 1955. 4 figs., 21 refs.

In 51 cases of retrolental fibroplasia, electroencephalographic recordings were obtained in the waking and sleeping states. Although only 27% of patients had some form of clinical epilepsy, seizure activity was present in 88% of the entire group (in 100% of those with seizures and in 70% of those without seizures). The clinical history of seizures and the occurrence of mental retardation suggested brain disorder in some cases, but the present study indicates that brain disorder may occur in cases of retrolental fibroplasia.

The frequency of seizure activity among younger and older children differed; 50% of those under and 97% of those over 3 years of age had seizure activity. The commonest electroencephalographic abnormality was a focus of spike-seizure activity in one or both occipital areas. This occurred in 35% of children under and 74% of those over 3 years of age. Follow-up studies on children with occipital-lobe foci have shown that this type of focus tends to disappear with increasing age or to migrate into the midtemporal region.

The following circumstances are considered possible causes of the seizure activity in retrolental fibroplasia: trans-synaptic degenerative changes in the brain secondary to blindness in early infancy (structural evidence of such changes has been reported by Von Gudden); oxygen poisoning of the immature brain resulting from excess oxygen in the respired air; and premature photic stimulation.—[Authors' summary.]

174. **The Relation between the Glycogen Content of Brain Tissue, as Demonstrated Histochemically in Biopsy Specimens, and the Frequency of Electrical Discharge.** (Über Beziehungen zwischen histochemischen Glykogenbefunden und der Hirnwellenfrequenz im EEG an einem Material von menschlichen Biopsien)

R. FRIEDE. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **194**, 213–237, 1956. 4 figs., bibliography.

The author cites various observations reported in the literature which provide evidence of an association between changes in the glycogen content of the brain, as demonstrable histochemically, and the occurrence of abnormal electrical potentials, an increase in the glycogen content apparently being accompanied by a reduction of wave frequency in the electroencephalogram (EEG). To test this hypothesis he examined specimens of cerebral cortex excised at operation in 32 cases of cerebral tumours, scars, abscesses, and other conditions treated at the University Neurosurgical Clinic, Freiburg im Breisgau, staining the tissue for glycogen by the McManus–Hotchkiss method and correlating the findings with the preoperative EEG.

Glycogen was mainly present in the perivascular spaces and interstitial and subpial tissue. It accumulated in Lamina I and in the valleys between the gyri without showing any preference for particular cell layers. Whatever the diagnosis, areas showing an increase in glycogen content corresponded to the foci of delta waves, those with slight or moderate amounts of glycogen to foci of waves of medium frequencies, and absence of glycogen to normal EEG findings. Age, duration of illness, intracranial pressure, and cerebrospinal-fluid findings were without significance. The glycogen present in the cortex was mainly localized in the glia, suggesting an increased intensity of metabolism in the interstitial and glial elements which may be presumed to influence the activity of the neurone. *W. Mayer-Gross*

175. **Cervical Vertigo**

G. M. S. RYAN and S. COPE. *Lancet* [*Lancet*] **2**, 1355–1358, Dec. 31, 1955. 18 refs.

The part played by the neck in the aetiology of vertigo is discussed with reference to the occurrence of vertigo in 2 patients after neck traction for symptoms due to bony disease of the cervical spine and in 3 patients (one of whom had cervical spondylosis) following accidental trauma to the neck. The injury in these 5 cases precipitated pain in the back of the neck and in the occipital region, this being associated in 3 instances with stiffness of the neck. At varying intervals of time after the injury each patient experienced recurrent attacks of vertigo, which were brought on particularly by lying down, looking up, and moving the neck. Vertigo and nystagmus could be reproduced in 2 patients by movements of the head relative to the neck, but when head and neck were moved as a whole these symptoms were not observed. Abnormal neurological signs included doubtful partial anaesthesia in the right forearm in one patient and weakness of the hand grip in another. General and aural examinations did not reveal any abnormalities, but radiographs of the cervical spine showed evidence of damage to the upper cervical vertebrae in 4 of the 5 cases. The patients obtained relief from symptoms by wearing a cervical collar; eventually 4 of the patients recovered completely.

The authors briefly review published reports of cases of vertigo occurring in association with cervical spondylosis, neck traction, or trauma, and discuss the mechanisms responsible for the symptoms. They suggest that trauma of the neck interferes with tonic neck reflexes, and that the proprioceptive impulses from the injured muscles and ligaments provide the cerebellum and the vestibular nuclei with "false information" resembling that from otolithic disease of the ear. Vertigo and nystagmus are then produced. The absence of neuro-

logical signs of damage to the central nervous system further supports the view that only peripheral end-organs are involved.

The authors propose that this syndrome should be called " cervical vertigo ". *Marcel Malden*

176. **The Finger-flexion Reflex in the Supine Position of the Forearm.** (О пальцевом сгибательном рефлексе при супинационном положении предплечья)
A. N. Shtempel'. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **56**, 33–35, No. 1, 1956. 2 figs., 5 refs.

Among the earliest signs of mild pyramidal lesions is a positive finger-flexion reflex described by Trömner in 1912 and commonly called Rossolimo's sign. As originally described, it is elicited by stroking the tips of the fingers with the forearm in the position of pronation and the hand hanging downwards. Venderovich's modification consists in eliciting this sign with the patient's forearm supine and the palm of the hand facing upwards.

The author, working at the Pavlov Medical Institute, Leningrad, has studied the reactions of 215 patients with minimal hemiparetic lesions and compared them with those of 1,449 normal controls to these and other tests for pyramidal lesions. While Rossolimo's sign was present in only 9·6% of the cases of hemiparesis, and then only in the third week after the injury or later, Venderovich's modification gave a positive result in 51·6%, in half of which it was elicitable within the first 3 days after the injury, and in nearly all within the first week. *Alexander Duddington*

177. **Studies in Myasthenia Gravis—a Rapid Diagnostic Test**
K. E. Osserman and P. Teng. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 153–155, Jan. 21, 1956. 1 fig., 6 refs.

This paper records further experience with the edrophonium (" tensilon ") chloride test for myasthenia gravis (Osserman and Kaplan, *J. Amer. med. Ass.*, 1952, **150**, 265; *Abstracts of World Medicine*, 1953, **13**, 421).

The test has been carried out at the Mount Sinai Hospital, New York, on 110 myasthenic patients and over 180 control subjects. Originally, 10 mg. of edrophonium in 1 ml. was injected intravenously in the course of 15 seconds, but the authors now advise the injection of 2 mg. in 15 seconds, followed 30 seconds later by an additional 8 mg. if no reaction occurs. The characteristic response in myasthenia gravis is an increase of strength in weak muscles, marked subjective improvement, minimal or absent side-reactions, and absence of muscle fasciculation. In normal subjects and patients with other types of muscle weakness there is no change in muscle power and fasciculation nearly always occurs. In 8 myasthenic patients in the authors' series, however, there was a false negative response in which muscle weakness was accentuated, fasciculation occurred, and there was flushing of the face, salivation, abdominal pain, and nausea. *J. W. Aldren Turner*

178. **An Electromyographic Study of Myotonia**
W. F. Floyd, P. Kent, and F. Page. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **7**, 621–630, Nov., 1955. 7 figs., 14 refs.

The authors report an extensive electromyographic investigation carried out at the Middlesex Hospital Medical School, London, in a case of myotonia atrophica with a pronounced myotonic component. Movement of the concentric needle electrode, percussion, voluntary activity, and electrical stimulation all led to prolonged after-discharge, at first at rates as high as 200 c.p.s. It is suggested that all forms of stimulus act in the same way, by deformation of muscle fibres which have an abnormally high mechanical irritability.

The effect of curare in preventing voluntary contraction without diminishing after-discharges, and the converse effects of appropriate doses of local anaesthetics, were confirmed, but the systemic injection of procaine hydrochloride had no effect [probably because of insufficient dosage, since Geschwind and Simpson (*Brain*, 1955, **78**, 81) have found the amide to be effective].

The defect resulting in increased irritability is thought to lie in the muscle-fibre membrane, a view [probably correct] which the authors have difficulty in reconciling with their belief that the after-discharge consists of motor-unit action potentials [which is open to question]. *William Cobb*

BRAIN AND MENINGES

179. **The Syndrome of Increased Intracranial Pressure without Localizing Signs**
L. Berg, H. L. Rosomoff, N. Aronson, M. Silbermann, and J. L. Pool. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **74**, 498–505, Nov., 1955. 4 figs., 1 ref.

From an examination of the records of the Neurological Institute of New York for the period January, 1945, to September, 1953, the authors found that of 2,000 patients subjected to ventriculography, 238 had raised intracranial pressure without localizing signs. According to the final diagnosis 117 (49%) of these had a laterally placed mass in one cerebral or cerebellar hemisphere, 62 (26%) had a midline obstructing lesion, 27 (11%) had " serous meningitis ", and 32 (14%) suffered from miscellaneous infective or vascular conditions, including malignant hypertension and communicating hydrocephalus. Of the laterally placed tumours, only 18 were cerebellar. A meningioma or a subdural haematoma was present in one-third of the cases of laterally-placed lesions without localizing signs. Of the cerebral-hemisphere tumours, 51 involved the minor hemisphere, 34 affected the dominant hemisphere, and 14 were bilateral. Omitting the miscellaneous group from the total, the percentage incidence of the other conditions was as follows: supratentorial lateral mass, 48; tumour in one cerebellar hemisphere, 9; obstruction of the third or fourth ventricle, 30; and serous meningitis, 13. It is of some interest that of the total number of cases of obstruction of the third ventricle in the

entire series of 2,000, nearly one-half presented with signs of raised intracranial pressure only, whereas similar signs were seen in only 2 of 143 patients with lesions in and around the sella.

The incidence of cases of laterally-placed tumour without localizing signs increased with age. Patients suffering from mental clouding were distributed among the three main groups—hemisphere lesions, midline obstruction, and serous meningitis—with the same frequency as patients who were alert. Plain radiographs were of considerable value in locating a laterally-situated lesion, conclusive signs being present in 22%. The electroencephalogram correctly indicated whether the lesion was lateral or central in 67% of cases.

Thus, the clinical syndrome of increased intracranial pressure without localizing signs or with only the commonly accepted false localizing signs is more often caused by a laterally-situated tumour of the hemispheres than by obstruction in the midline or by serous meningitis. The implication of this, so far as methods of investigation are concerned, is obvious. The problem of how a laterally-placed lesion can be large enough to cause increased intracranial pressure and yet not give rise to localizing signs remains unsolved. [Unfortunately the authors give no information concerning the rate at which the tumours developed.] *J. Foley*

180. **Residual Function following Hemispherectomy for Tumour and for Infantile Hemiplegia**
W. J. GARDNER, L. J. KARNOSH, C. C. MCCLURE, and A. K. GARDNER. *Brain* [*Brain*] **78**, 487–502, 1955. 25 refs.

The authors have compared the long-term changes in psychological make-up and in the motor, sensory, and speech functions in two groups of patients subjected to hemispherectomy. In the first group, consisting of 10 patients studied by the authors at the Cleveland Clinic, Cleveland, Ohio, the operation was performed for the removal of a glioma—the relevant clinical data are presented in a table—while in the second, consisting of 54 cases collected from the literature, hemispherectomy was performed for infantile hemiplegia. A brief summary is provided of the findings of each authority quoted, to which the authors add a detailed clinical analysis of one case of infantile hemiplegia seen by themselves.

The comparison showed that in patients with infantile hemiplegia there was, after operation, no increase in the pre-existing impairment of motor or sensory function, while improvement occurred in some cases and there was freedom from convulsive seizures in most. No exact information on speech function was available in the reported histories. Psychological studies showed improvement in emotional control, attentiveness, and powers of concentration, accompanied by relief from temper tantrums; there was no evidence of intellectual deterioration.

In contrast, the patients subjected to hemispherectomy for glioma showed a spastic hemiparesis which tended not to improve with time, and there was impairment of all types of sensation. Disturbances of language were not serious unless the dominant hemisphere was resected—but handedness was not always a safe indication of the side of dominance. In almost all cases there were personality changes, with defects of judgment and impairment of insight, emotional control, initiative, and perseverance.

From this study the authors conclude that if a hemisphere is damaged before birth or in early infancy other parts of the brain can take over its functions, but that this does not occur at a later stage of development. In the authors' own words " the immature cortex of one hemisphere can *acquire* functions which nature planned for the cortex of the other side, but (with the possible exception of speech) once a function has become established in the cortex, it cannot be *transferred.* Since corticalization of function is an ontogenetic as well as a phylogenetic phenomenon, the infant can part with his cortex with less resulting functional deficit than can an adult.". *Marcel Malden*

181. **Electroencephalographic and Clinical Observations in Boxers, and their Significance in the Morbid Physiology of Brain Injuries.** (Elektrencephalographische und klinische Befunde bei Boxern und ihre Bedeutung für die Pathophysiologie der traumatischen Hirnschädigung) F. PAMPUS and W. GROTE. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **194**, 152–178, 1956. 8 figs., bibliography.

This paper records the findings in serial electroencephalograms (EEGs) taken on 250 active amateur boxers and 17 retired professionals. Over 500 EEGs were examined and a clinical neurological examination was carried out in 175 cases.

The average incidence of abnormal findings in tracings made before a fight was 29%. This figure increased markedly in tracings taken within a week after one or several fights: after three fights, for example, it rose to 42%. The frequency of pathological findings was clearly correlated with the frequency and number of fights. A knock-out was followed by severe transitory changes in the EEG, but was by no means a prerequisite for the development of definite pathological changes. In addition to transient abnormalities, certain changes were found to last for several days after a fight, in some instances even increasing in intensity after 3 or 4 days. Chronic trauma of this kind seems to leave behind a greater susceptibility to further injury and a failure of the brain to compensate for small interferences with its function, so that a normal EEG and normal clinical findings are no guarantee of the functional and anatomical integrity of the brain in such cases. This applies especially to juvenile boxers who, in the present series, showed greater vulnerability than the adults. Fights repeated at a time when the changes resulting from preceding fights have not yet disappeared may be especially harmful. In addition to the direct mechanical trauma to the brain caused by blows on the head, reflex disturbances of the circulation caused by blows in the region of the carotid body and heart are held responsible for the abnormalities found clinically and in the EEG.

[This is a very careful and thorough study which takes account of the more important international contribu-

tions to the literature of the subject. The discussion of the clinical significance of the findings and of the traumatic mechanisms involved is worth reading in full, being intelligent and comprehensive and only occasionally rather verbose and unnecessarily involved.]

W. Mayer-Gross

182. **Observations on the Mechanism of Brain Concussion, Contusion, and Laceration**

E. S. GURDJIAN, J. E. WEBSTER, and H. R. LISSNER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 680–690, Dec., 1955. 7 figs., 14 refs.

Cerebral concussion is an acute post-traumatic state associated with unconsciousness, pallor, and a shock-like state and is the result of derangement in function of the brain stem. The brain stem involvement may be of varying degree involving both reversible or irreversible damage. The reversible state may result in complete recovery; the irreversible, in unconsciousness with ultimate death. Concussion may be associated with brain contusions and lacerations or it may be unaccompanied by macroscopic evidences of injury to the neural tissue. Contusions and lacerations of the brain may be unaccompanied by concussion.

The closed cavity dynamics of the head may be disturbed by injuries resulting in major damage with or without concussion. The closed cavity dynamics in many injuries is the cause of unconsciousness and death. Both are due to physical forces deranging the brain stem function. Concussion occurs as a result of brain stem injury either from increased intracranial pressure at the time of impact, direct injury by distortion, mass movement, shearing, or destruction by a missile.

The terms cerebral concussion, contusion, and laceration should not be used to denote varying degrees of nervous system damage, with concussion identified as representing the mildest form. The evidence indicates that concussion is due to an involvement of a specific area of the brain, namely the brain stem. A contusion or laceration in this area may be fatal. However, contusions and lacerations in other portions of the nervous system may be present with no associated concussive effect if the brain stem area is not sufficiently involved. —[Authors' summary.]

183. **Mechanisms in the Production of Hemiparesis Associated with Intracranial Aneurysm**

W. E. STERN. *Brain* [*Brain*] **78**, 503–513, 1955. 9 figs., 27 refs.

From a review of the literature on the subject of hemiparesis associated with intracranial aneurysm, and a personal study of 6 such cases seen at Wadsworth General Hospital (University of California), Los Angeles, the author suggests that intracranial aneurysm may give rise to hemiparesis as a result of any of the following conditions. (1) Compression of the brain substance due to extracerebral, subarachnoid effusion of blood; no actual cases of local brain damage from this cause have been published, but it has been suggested that subarachnoid blood effusions can provoke focal neurological signs. (2) Intracerebral haemorrhage resulting from rupture of the aneurysm; there were 2 such cases in the author's series. (3) Subdural haemorrhage; this may occur as a complication of subarachnoid haemorrhage, but probably is not the major factor in production of hemiparesis in these circumstances. (4) Embolization from the aneurysmal sac; although such an occurrence is theoretically possible the author could not find any proven examples. (5) Compression of the brain substance by the unruptured aneurysm acting like any other space-occupying mass; in such cases the crus cerebri appears to be the part most frequently affected. (6) Occlusion of the parent artery by thrombosis spreading from the aneurysmal sac. Such occlusion may occur with or without rupture of the aneurysm; in the latter case the patient may present with the clinical picture of cerebral thrombosis, and the presence of aneurysm as the underlying cause may not be suspected. The author stresses the importance of this possibility, especially when cerebral thrombosis occurs in young people; the description of his third case well illustrates these difficulties. (7) Insufficiency of the carotid system, which may result from vascular spasm or partial compression by the aneurysmal sac, or may be causally connected with the development of cerebral oedema; this mechanism was responsible for the hemiparesis in the remaining 3 of the author's cases.

Marcel Malden

184. **Hypothermia, and Interruption of Carotid, or Carotid and Vertebral Circulation, in the Surgical Management of Intracranial Aneurysms**

E. H. BOTTERELL, W. M. LOUGHEED, J. W. SCOTT, and S. L. VANDEWATER. *Journal of Neurosurgery* [*J. Neurosurg.*] **13**, 1–42, Jan., 1956. 20 figs., 21 refs.

The authors describe the results in 22 cases operated upon at Toronto General Hospital during 1954–5 at varying periods after rupture of an intracranial aneurysm, in which hypothermia was employed to minimize the effects of cerebral anoxia. Temporary occlusion of the great vessels of the neck bilaterally or in varying combinations was employed when made necessary by bleeding from the aneurysm or an adjoining artery.

Hypothermia was produced by immersing the patient in a bath containing ice water. Anaesthesia was induced with chlorpromazine, promethazine, and pethidine administered by intravenous drip and was maintained with nitrous oxide, oxygen, and trichlorethylene (thiopentone is not now used). The authors regard 30° C. (86° F.) as the optimum temperature for operation, the temperature being recorded on a thermocouple inserted into the rectum and deep in the thigh muscle. Continuous electroencephalography was carried out during the intracranial procedure; when this was completed, rewarming with water at 35° C. (95° F.) was begun if the rectal temperature was below 30° C. or still falling; otherwise spontaneous rewarming was allowed to take place. The common carotid and vertebral arteries were exposed bilaterally in the neck. If occlusion became necessary a rubber-covered " bulldog " clamp was placed on the carotid arteries, the vertebral arteries being compressed digitally against the transverse process by an assistant. It is considered that 6 minutes of cerebral

ischaemia at 30° C. should be well tolerated, but the period of safety varies from case to case and the best guide is the electroencephalogram.

Postoperatively the blood pressure, pulse rate, respiratory rate, and temperature were noted every 15 minutes. The warning is given that a dangerous degree of systemic hypotension may occur, requiring the intravenous injection of noradrenaline. In some of the authors' cases the development of any respiratory difficulty postoperatively was treated immediately by tracheotomy.

Of the 22 patients, 3 died; in the 19 survivors the result was judged to be " excellent or good " in 16, " fair " in one, and " bad " in 2. Detailed case reports are given on each of these patients, including the operative detail, and there is discussion of the electrocardiographic findings, the usefulness of the electroencephalogram, and the " safe " period of cervical arterial occlusion. It is the authors' opinion that the results of surgery of intracranial aneurysms in this series of cases have been improved by the use of hypothermia.

[This is a most important paper that calls for study by all surgeons who practise the intracranial attack on berry aneurysms.] *J. V. Crawford*

185. **Excision of Occlusive Lesions of the Middle Cerebral Artery**

K. WELCH. *Journal of Neurosurgery* [*J. Neurosurg.*] 13, 73–80, Jan., 1956. 6 figs., 11 refs.

The degree of infarction following obstruction of the middle cerebral artery or one of its branches appears to depend on factors that come into play after the occlusion; among these are propagation of blood clot proximally into the region of origin of the branches penetrating the area of cortex affected and also the efficiency or inefficiency of the collateral circulation, the rapidity with which this circulation is brought into play being of vital importance. The balance between the state of the general circulation and the efficiency of the surface anastomoses between the cerebral arteries is a precarious one. Definite advantages might therefore be expected to follow if it were possible to re-establish the blood flow through the middle cerebral artery.

In this paper from the University of Colorado, Denver, the author describes an attempt to relieve such occlusive lesions in the middle cerebral artery in 2 patients. The first was a 47-year-old man who had shown some recovery from hemiplegia after thrombosis of the right middle cerebral artery; 4 weeks after onset this artery was incised, the thrombus removed, and the vessel closed. Subsequently the ascending branches of the middle cerebral artery were demonstrated by arteriography to be patent. The patient has had good recovery of function except for finger dexterity. The second patient was a woman aged 51 who was suffering from auricular fibrillation and who was operated upon 12 hours after being found with right hemiplegia and aphasia, when an embolus was excised from the left middle cerebral artery. In this case, however, the neurological status has not improved, and subsequent arteriography revealed renewed obstruction of the middle cerebral artery. *J. V. Crawford*

186. **Evaluation of Current Therapy in Cerebral Vascular Disease**

J. F. FAZEKAS, J. KLEH, and R. W. ALMAN. *Journal of Chronic Diseases* [*J. chron. Dis.*] 2, 508–519, Nov., 1955.

We have reviewed the therapeutic effectiveness of vasodilating agents, stimulants, anticoagulants, and hypotensive agents, as well as rehabilitative procedures, in patients with cerebral vascular disturbances. With the exception of carbon dioxide, vasodilators available at the present time do not increase total cerebral blood flow, and they cause relaxation of cerebral vessels only in association with a reduction of pressure. The rapid development of brain damage following ischemia makes it unlikely that therapy directed toward increasing cerebral blood flow would have any practical value in chronic cases. The effectiveness of cerebral stimulants in patients with cortical dysfunction and generalized cerebral vascular disease is questionable from both physiologic and clinical evidence currently available.

The presence of overt manifestations of cerebral vascular disease (thrombosis) does not militate against the use of hypotensive agents. Blood pressure should, however, be gradually reduced and maintained somewhat above normal values. Anticoagulants are effective in reducing significantly the incidence of cerebral emboli in patients with rheumatic heart disease and myocardial infarction as well as recurrent attacks from threatened occlusion of basilar and carotid arteries. Experience with these drugs in patients with cerebral thrombosis is limited. There is little justification for their use in patients with psychosis and cerebral arteriosclerosis.

Although rehabilitative procedures at present seem to be the most valuable of all therapies available to patients with cerebral vascular disease, most existing programs are incomplete or are very costly. There is a great need for the establishment of rehabilitation boards in hospitals. —[Authors' summary.]

EPILEPSY

187. **An Electroencephalographic Study of the Near Relatives of Epileptic Patients.** (L'électroencéphalographie chez les proches parents d'épileptiques)

P. VERCELLETTO. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] 7, 585–596, Nov., 1955. 8 figs., 12 refs.

The electroencephalograms (EEGs) of the near relatives of 109 patients with idiopathic and 107 with symptomatic epilepsy were studied at the Neurological Centre of the Nantes Hospitals. In 45 cases in the former group both parents were examined: paroxysmal discharges were found in both parents in 15% and in one parent in 60% of these cases. The proportion of abnormalities in the EEG was as high as 85% in at least one parent if non-paroxysmal features were included. In 49 cases only one parent was examined, and in 15 only siblings, a high proportion of abnormal records being found, though clinical epileptic manifestations were very uncommon. Paroxysmal EEG activity rarely occurred spontaneously, but could be evoked by

overbreathing or photic stimulation. Close morphological resemblance between the paroxysmal discharges of the patients and of their near relatives was noted.

In 8 cases in patients with "symptomatic" epilepsy who had no family history of the disease paroxysmal discharges were found in the EEG of one parent. These were bilaterally synchronous, in contrast to the localized abnormalities seen in the patient's EEG.

The dominant or recessive nature of the inheritance of epilepsy and the importance of a predisposition in some cases of symptomatic epilepsy are discussed.

William Cobb

188. **The Rhythm of Epileptic Attacks and its Relationship to the Menstrual Cycle.** [In English]
R. ALMQVIST. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] Suppl. 105, 1–116, 1955. 37 figs., 29 refs.

189. **Vestibular Epilepsy**
S. BEHRMAN. *Brain* [*Brain*] **78**, 471–486, 1955. 29 refs.

The author discusses the type of epilepsy which is associated with a vertiginous aura, post-ictal vertigo, or inter-ictal paroxysmal vertiginous disturbances, basing his observations on the clinical analysis of 39 cases seen at three London hospitals. The vestibular origin of the vertigo, associated in some cases with tinnitus, deafness, or disequilibrium, was assumed from consideration of the case histories; the epileptic manifestations consisted in loss of consciousness with or without convulsive movements. As the author writes: "If the vestibular origin of pre- and post-ictal vertigo is accepted, the ictus also can be reasonably regarded as having been precipitated by the vestibular activation, and 'vestibular epilepsy' is the suggested designation of this nosological entity". The histories of 11 selected cases are presented in detail to illustrate the three broad subdivisions of the syndrome: (1) cases with post-ictal vertigo only; (2) those with pre-ictal and inter-ictal vertigo; and (3) those with vestibular symptoms between seizures and independently of them. (No attempt was made to establish the pathological nature of the labyrinthine disorders, the author feeling that the knowledge of the pathology of the labyrinth at present available would not make this rewarding.)

A distinction is drawn between vestibular epilepsy and epilepsy with an acoustic or vertiginous aura, the former being differentiated from the latter (1) by its association with a more violent and rotatory type of vertigo, (2) by the absence of other hallucinations of the special senses, (3) by the absence of enduring post-ictal focal symptoms, and (4) by the presence of inter-ictal labyrinthine disturbances. Discussing the mechanism of production of vestibular epilepsy the author suggests that the seizure is provoked in certain circumstances in constitutionally predisposed individuals by excessive spontaneous discharge from the vestibular apparatus. Thus vestibular epilepsy would form a sub-group of the sensorily precipitated epilepsies. It was unfortunately not possible to obtain an electroencephalographic recording during a spontaneous attack in any of the patients, nor could the seizures be precipitated by caloric stimulation. Of 13 resting electroencephalograms analysed, 7 were classed as normal and 6 as epileptic.

Marcel Malden

190. **The Electroencephalographic Concomitants of Experimental Subcortical Epilepsy.** [In English]
W. H. FAETH, A. E. WALKER, and W. A. WARNER. *Acta neurológica latinoamericana* [*Acta neurol. latinoamer.*] **1**, 239–255, 1955. 16 figs., 34 refs.

SPINAL CORD

191. **Early Diagnosis of Compression of the Spinal Cord by Neoplasms**
G. F. ROWBOTHAM. *Lancet* [*Lancet*] **2**, 1220–1222, Dec. 10, 1955. 1 ref.

Between 1941 and 1948, 80 cases of neoplastic compression of the spinal cord came under the care of the author at the General Hospital, Newcastle upon Tyne. An intramedullary glioma was found in 6 cases; in the remaining 74 the tumour was extramedullary, the types and the numbers of patients affected being as follows: meningioma (14 patients); neuroma (22); angioma (5), tumours of the cauda equina (5) (giant-cell 2, ependymoma 2, embryoma 1); osteoclastoma (3); osteochondroma (1); chondrosarcoma (3); lymphosarcoma (1); secondary carcinoma (20). Presenting symptoms varied considerably in severity, and included pain or loss of sensation, muscle weakness or paralysis, sphincter paralysis, and renal infection. The neurological signs were much the same regardless of the nature of the neoplasm, except that in cases of cancer paralysis often developed rapidly after the initial weakness, while in cases of compression due to a benign tumour paralysis developed slowly. *X*-ray examination was not always helpful, and in some cases the reaction to the Queckenstedt test was negative. The importance of early diagnosis and the difficulties encountered are emphasized. Persistent pain of root distribution, especially if aggravated by straining and coughing, and a slight increase in the protein content of the cerebrospinal fluid (up to 60 mg. per 100 ml.) are suggestive findings. It is further emphasized that an underlying embryoma should be suspected where there is spina bifida associated with progressive cord compression at the corresponding level.

A. Wynn Williams

192. **Diagnosis and Treatment of Myelopathy Due to Cervical Spondylosis**
D. W. C. NORTHFIELD. *British Medical Journal* [*Brit. med. J.*] **2**, 1474–1477, Dec. 17, 1955. 2 refs.

Cervical spondylosis may lead to changes in the spinal cord conveniently termed myelopathy, in which compression of the cord by intraspinal osteophytes and ischaemia by interference with its blood supply both play a part to an unknown degree. The results of 39 cases of spondylotic myelopathy treated by operation are reviewed. The duration of the symptoms varied between 6 weeks and 20 years, and the ages of the patients ranged from 30 to 70 years.

Disturbance of function of the cervical spine was insignificant. Weakness or stiffness of one or both legs was the commonest initial symptom—present in 15 cases. In the upper limbs, weakness, wasting, flaccidity or spasticity, and increase or decrease of tendon reflexes occurred in all but 2 cases. In the lower limbs there was moderate to marked spastic weakness in 27 cases. Sensory disturbances of all varieties occurred in the majority of cases; detection of these, however, may need care. Disturbances of micturition, rarely severe, occurred in only a minority.

Radiography, including myelography, is essential for diagnosis. Osteophytes may be present at only one level or may be widely distributed, in the latter event producing an extensive cord lesion. Operation comprised laminectomy, the arch above and below the disk being removed. The ligamenta denticulata have also been divided, and where necessary the intervertebral foramina have been enlarged. In 3 cases spinal fusion was carried out.—[Author's summary.]

193. **A Survey of the Neurological Results of 858 Spinal Cord Injuries. A Comparison of Patients Treated with and without Laminectomy**

A. E. COMARR and A. A. KAUFMAN. *Journal of Neurosurgery* [*J. Neurosurg.*] **13**, 95–106, Jan., 1956. 18 refs.

The large number of patients admitted to the paraplegic service of the Veterans Administration Hospital, Long Beach, California, has given the authors an unusual opportunity to study the important question of when laminectomy is indicated in the management of spinal-cord injuries. Review of a series of 858 cases of spinal-cord injury showed that laminectomy was performed in 579 at various intervals after injury, while in 279 cases operation was not performed. The degrees of neurological recovery in these two groups are compared.

Of the 579 laminectomized patients, 91 (16%) were significantly improved postoperatively and 47 (8%) were eventually able to walk, between 1 and 2% without aids. Of the patients not operated upon, 80 (29%) were improved neurologically, and 44 (16%) were ambulatory, 6% without aids.

It is pointed out, however, that in many cases the laminectomized patients had graver injuries than those not subjected to laminectomy. In both categories the intraspinal nerve lesions recovered more frequently than the spinal cord lesions. This was thought to indicate a greater tolerance of trauma in the nerves of the cauda equina rather than a greater capacity for regeneration. In both groups it was found that systems conducting tactile sensibility recovered most frequently, pain and temperature sensibility and motor function returned next most frequently, while bladder sensation and motor control recovered least frequently of all functions. Among the laminectomized patients the most favourable interval between injury and operation ranged from 24 hours to one month; those operated upon earlier seemed less likely to improve if they had spinal-cord lesions. A lower rate of improvement was observed in all types of lesion operated upon more than one month after injury.

The presence of spinal subarachnoid block was an important factor, influencing prognosis adversely. Patients with complete block who were not operated upon did not improve. The gross appearance of the cord at operation gave no reliable indication of prognosis, unless of course the cord was obviously transected. Many patients described as having an apparently normal cord did not improve, whereas many with subtotal lesions did improve. The indications for and against laminectomy are discussed, the authors concluding as follows: (1) the presence of subarachnoid block is a strong indication for decompression; (2) the absence of subarachnoid block is in favour of initial conservative treatment (anterior cord compression is discussed in the light of the above); (3) laminectomy performed as long as one year after injury may in rare cases afford some improvement in those with complete block, but if delayed longer it is probably only of psychological benefit to the patient. *J. V. Crawford*

194. **The Babinski Response: a Review and New Observations**

P. W. NATHAN and M. C. SMITH. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 250–259, Nov., 1955. 7 figs., 39 refs.

The extensor plantar response described by Babinski is commonly regarded as one of the most constant manifestations of a lesion in the cortico-spinal (pyramidal) system. The validity of this view is re-examined in this important article, the first part of which is devoted to a brief review of the literature, including the observations of Babinski himself. It emerges that early pronouncements linking the sign with lesions in the cortico-spinal tract were not adequately supported by anatomical evidence. Thus the sign was absent in some cases in which the spinal cord was totally divided and in others with clearly demonstrable lesions in the cortico-spinal tract. The nature of the plantar response is known to change from flexor (" negative ") to extensor (" positive ") and vice versa in the same patient. It may also be present, on occasions, in individuals with a normal motor system, during sleep, hypoglycaemia, and general anaesthesia, after the injection of hyoscine, and after epileptic fits.

In the second part of the paper the authors present their own observations, made at the National Hospital, Queen Square, London, before and after antero-lateral cordotomy for the relief of pain in 38 cases of incurable cancer. When the presence or absence of a positive response was correlated with the position of the surgical lesion it was found that lesions in the lateral or ventral columns of the cord were not always associated with a positive response, and that the latter was sometimes present in cases in which the cortico-spinal tracts remained intact. There was, in other words, " no particular relation between the anatomical state of the cortico-spinal tracts and the form of the plantar response ". While there is thus no justification for associating the sign narrowly with lesions in the cortico-spinal tract, it remains nevertheless a valuable indication of abnormal function of the central nervous system. *L. Crome*

Dermatology

195. **The Water Content of the Stratum Corneum. III. Effects of Previous Contact with Aqueous Solutions of Soaps and Detergents**

I. H. BLANK and E. B. SHAPPIRIO. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **25**, 391–401, Dec., 1955 [received March, 1956]. 5 figs., 6 refs.

The dryness of the skin which follows repeated contact with soap and synthetic detergent solutions may be due to the removal of hydrophilic materials from the skin. In experiments carried out at the Massachusetts General Hospital (Harvard Medical School), Boston, it was shown that thin sheets of callus cut from the sole of the foot became less flexible after soaking in water or in solutions of detergents. The water-holding capacity of horny epithelium was not much reduced by soaking in water but it was considerably reduced by soaking in solutions of soap or synthetic detergents. This reduction was unaffected by the addition of sodium triphosphate (commonly present in household soaps and detergents) to the solutions. It was also shown that water and solutions of detergents could extract nitrogenous material, including aromatic amino-acids, from calluses or from cornified epithelium. A solution of sodium triphosphate extracted more nitrogenous material than did water, and the addition of alkali to the detergent solutions increased the extraction of nitrogen. By the technique used synthetic detergents could not be shown to be more damaging to cornified epithelium than coconut oil soap. *E. Lipman Cohen*

196. **Lupus Erythematosus. Clinical and Hematological Studies in Seventy-seven Cases**

R. H. MARTEN and E. K. BLACKBURN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 1–14, Jan., 1956. 35 refs.

The clinical and haematological features of cases of lupus erythematosus seen in the Sheffield area between 1948 and 1952 are discussed. There were 77 cases during this period, including 66 of chronic discoid, 6 of generalized discoid, 4 of subacute disseminated, and one case of acute disseminated lupus erythematosus. The age at onset in the chronic discoid cases varied from 12 to 67 years, with maximum incidence between ages 20 and 44. The condition had been present for less than 10 years in most cases. Except for local trauma in 3 cases of chronic discoid and exposure to sunlight in one case of subacute disseminated disease there were no specific precipitating factors. Sunlight, however, aggravated the condition in 41 cases of chronic discoid, 4 of generalized discoid, and 2 of subacute disseminated lupus erythematosus. In addition to the cutaneous lesions there were transient joint pains in 12 of the patients in the chronic discoid group, 2 of those with generalized disease, and 2 with the subacute disseminated form. Myalgia was present in 2 cases of chronic discoid disease, while in 5 cases in this group there was significant loss of weight. The spleen was palpable in 2 male patients with chronic discoid lupus erythematosus and there was hepatomegaly in one with generalized discoid disease without other constitutional disturbance.

On haematological examination a microcytic, hypochromic anaemia was found in 3 females and 1 male with chronic discoid disease, but there were no cases of haemolytic anaemia. Leucopenia was observed in 5 and thrombocytopenia in 2 cases in this group, and in 24 others the erythrocyte sedimentation rate was raised. Also in this group were 3 cases in which cold agglutinins were present in varying titre and 2 in which the reaction to the direct Coombs test was positive. L.E. cells were found in the peripheral blood in 9 cases of chronic discoid, 2 of generalized discoid, 4 of subacute disseminated, and one of acute disseminated disease. In summary, in addition to the expected findings in the subacute and acute cases, some haematological abnormality was found in 36 cases of chronic discoid and 5 of generalized discoid lupus erythematosus.

These and other published findings are discussed. The authors state that it was not found possible to forecast clinically the cases in which haematological abnormalities might be found, and they conclude that the significance of these abnormalities can be assessed only after prolonged follow-up. *Benjamin Schwartz*

197. **Lupus Erythematosus Profundus. Commentary and Report of Four More Cases**

H. L. ARNOLD. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 15–33, Jan., 1956. 12 figs., 36 refs.

In lupus erythematosus profundus, a relatively uncommon clinical form of lupus erythematosus, the cutaneous infiltrate occurs primarily in the deeper portion of the corium and gives rise to firm, sharply-defined nodules varying up to several centimetres in diameter lying beneath comparatively normal skin. In this paper the literature is reviewed, particularly reports concerning the association with lupus erythematosus of subcutaneous nodules and plaques usually described as "sarcoid". The author then describes 4 cases occurring in females in the native population of Hawaii. In 3 cases the nodules were on the cheeks and in one in the deltoid region.

A summary of the histopathological findings shows the chief characteristics to be hyperkeratosis, follicular plugging, epidermal atrophy with loss of rete pegs, oedema of the basal cells, and an infiltrate around the appendages in the corium. Necrobiosis of collagen and fat and fibrinoid alteration of the collagen are also observed.

The differential diagnosis is from Darier–Roussy sarcoid, lupus erythematosus hypertrophicus et profundus in which there are marked epidermal changes, and the

Spiegler–Fendt "sarcoid" form of lymphoblastoma. The relationship between the nodules of lupus erythematosus profundus and the transitory nodules occurring in the vicinity of joints in some cases of systemic lupus erythematosus is not clear, but in the reported cases the nodules were persistent and remote from joints, and systemic involvement was not noted.

The paper includes reproductions of photomicrographs of tissue from the 4 cases described.

Benjamin Schwartz

198. **Some Aspects of the Physiological Effects of Cortisone in the Treatment of Pemphigus Vulgaris**

J. NEILL. *British Journal of Dermatology* [*Brit. J. Derm.*] 67, 434–443, Dec., 1955. 3 figs., 16 refs.

In order to illustrate the different effects of ACTH and cortisone in an individual case the author presents, from the Victoria Infirmary, Glasgow, the detailed case report of a woman aged 54 who had suffered from pemphigus vulgaris for 2½ years and who was treated for 2 years with cortisone or ACTH.

The first course of treatment, with 100 units of ACTH daily for 13 days, 75 units for one week, 50 units for one day, and 25 units for 3 days, resulted in a partial remission of the condition, followed by an immediate relapse on withdrawal of the hormone after 25 days owing to shortage of supplies. Cortisone (150 mg. daily) was then given and kept the patient free from lesions but, because adrenal depression was feared, 80 units of ACTH gel were substituted for the cortisone and an immediate relapse followed. She was then treated with both ACTH and cortisone, and once more there was a remission. In all, four courses of ACTH were given, each resulting in a relapse which was ended only by further administration of cortisone.

An estimation of adrenal function was made, based on the excretion of 17-ketosteroids. Evidence that there is adrenocortical damage in pemphigus vulgaris is presented and it is suggested that, as a result, treatment with ACTH is unreliable. Adrenal depression from cortisone treatment is thought to be much greater than is generally appreciated, and a sudden change from cortisone to ACTH is likely to be followed by a relapse, or even by adrenal failure if the disease has been present for a long time. Thus a "boosting" course of ACTH to maintain the adrenocortical secretion is a risky procedure.

It is concluded, therefore, that cortisone is the drug of choice in the treatment of pemphigus vulgaris.

S. T. Anning

199. **Nylon Stocking Dermatitis**

C. D. CALNAN and H. T. H. WILSON. *British Medical Journal* [*Brit. med. J.*] **1**, 147–149, Jan. 21, 1956. 4 figs., 6 refs.

Although nylon is widely used, sensitization to it is rare. Dermatitis due to nylon stockings is characteristically localized to the dorsum of the foot and the toes, in the popliteal fossa, and on the medial aspect of the thigh; more rarely, the heels and the soles are involved. Dermatitis due to a nylon hair-net may be localized behind the ears, on the forehead, or on the nape of the neck. The eruption is usually symmetrical, and may be acutely vesicular and weeping, or red and desquamating. In most instances the affected subjects are sensitive to the dye employed, which may be an azo or an anthraquinone dye, usually the former in Britain. The sensitizing factor is an amino group in the *para* position on the benzene ring.

In this paper from St. John's Hospital for Diseases of the Skin and the Royal Northern Hospital, London, 6 cases are reported. All the patients were sensitive to the yellow dye in nylon material, 4 also to the red, and one to black and to blue. The authors point out that while cross-reactions to other commonly used substances containing the *para*-amino grouping are rare, these substances should be borne in mind when patch tests are performed. Cross sensitivity to *para*phenylenediamine was observed in one of the authors' cases. Another possible cause of dermatitis from nylon stockings is the coating of synthetic resins which is designed to provide the so-called "snag" finish; such resins are, however, readily removed by washing.

At the authors' instigation one manufacturer has undertaken to use anthraquinone dye in nylon articles; no instance of sensitization to this substance has yet been encountered.

F. Hillman

200. **Necrobiosis Lipoidica**

P. J. HARE. *British Journal of Dermatology* [*Brit. J. Derm.*] **67**, 365–384, Nov., 1955. 4 figs., bibliography.

In the first part of this paper from University College Hospital, London, the author reviews some of the literature relating to necrobiosis lipoidica diabeticorum. He discusses the aetiology of the lesions, pointing out that similar clinical lesions have been reported in non-diabetic patients. He then proceeds to consider certain other morphological variants which also show the histology of necrobiosis; these include a condition very similar to granuloma annulare, and the conditions of necrobiosis maculosa and "granulomatosis disciformis"—a doubtful aetiological entity. Thus similar clinical and histological pictures are seen in association with: (1) diabetes mellitus, perhaps in relation to disordered fat metabolism; (2) obliterative changes in the dermal blood vessels, in the absence of diabetes or discernible abnormality of fat metabolism; and (3) purely inflammatory histological changes. The author feels, therefore, that it is impossible to be certain whether these skin conditions with clinical or histological similarities are manifestations of the same disease or whether the inflammation causes the vascular damage, or vice versa.

In the second part of the paper the author discusses the possible part played by glycogen and alkaline-phosphatase activity in the aetiology of these diseases. He has found that dermal deposits of glycogen were present in all of 9 cases of necrobiosis lipoidica diabeticorum examined, in 5 cases of necrobiosis in non-diabetics, and in 3 cases of necrobiosis maculosa. Glycogen was also found in 10 out of 12 cases of granuloma annulare, but generally in smaller quantities. It was not found in other cases of dermal or hypodermal inflammation, except in those showing necrosis or acute

inflammatory changes. The occurrence of glycogen did not seem to be specifically related to the presence of diabetes or of fatty, vascular, or inflammatory changes, or to degeneration or fibrosis. Its presence, therefore, does not throw any light on the problem whether the pathogenesis of necrobiosis lipoidica is primarily degenerative or primarily inflammatory. It appears, however, that necrobiosis lipoidica diabeticorum, necrobiosis lipoidica in non-diabetics, and necrobiosis maculosa are closely similar in pathogenesis and that in this respect all three differ from granuloma annulare.

Only 15 cases were examined for the presence of alkaline-phosphatase activity. The enzyme was, in general, found at sites similar to those in normal skin and also in areas of early fibrosis; its distribution thus did not suggest that it had any significance peculiar to necrobiosis. *Benjamin Schwartz*

201. **Impetigo Contagiosa. The Association of Certain Types of *Staphylococcus aureus* and of *Streptococcus pyogenes* with Superficial Skin Infections**

M. T. PARKER, A. J. H. TOMLINSON, and R. E. O. WILLIAMS. *Journal of Hygiene* [*J. Hyg.* (*Lond.*)] **53**, 458–473, Dec., 1955. 28 refs.

An investigation among young soldiers at Cambridge in 1941–2 demonstrated that of 298 cases of impetigo, *Staphylococcus aureus* was present alone in 158 cases and in association with haemolytic streptococci in 134. The ability to inhibit growth of *Corynebacterium diphtheriae* on solid medium was found in 47% of the strains of *Staph. aureus*. A more recent investigation carried out at Salford in 1953–4 among 190 Lancashire schoolchildren with impetigo showed that *Staph. aureus* was present in 83% of the cases, being the only pathogenic organism in 44%. Phage-typing revealed that three-quarters of the strains were of one variety, being susceptible to Phage 71.

In both investigations the variety of *Staph. aureus* was not commonly found in other superficial lesions, and was absent in deep lesions. Nearly 90% of Phage-71 *Staph. aureus* (and very few others) produced a narrow, sharply defined inhibition of growth of *Corynebacterium*. The majority of the staphylococci were penicillin-resistant, most being of Type 71. Most of the strains of *Streptococcus pyogenes* isolated in the Lancashire investigation were only identifiable by the slide-agglutination method. Two groups accounted for 78% of strains, and these were not commonly found in other lesions. *E. H. Johnson*

202. **Clinical and Bacteriological Aspects of Impetigo Contagiosa**

G. I. BARROW. *Journal of Hygiene* [*J. Hyg.* (*Lond.*)] **53**, 495–508, Dec., 1955. 31 refs.

Of 106 bacteriologically positive cases of impetigo studied at the Public Health Laboratory, Bradford, during 1953–4, culture studies gave a growth of *Staphylococcus aureus* in 100 cases; in 86 cases this was the only organism found, while a mixed growth containing also haemolytic streptococci was obtained in 14 cases. Of these 100 strains of *Staph. aureus*, phage-testing showed 63 to be of Type 71 and a further 17 to be closely related (" weak 71 "), whereas of 164 strains of *Staph. aureus* isolated from 200 control subjects only one strain was of Type 71 and 9 of " weak 71 ". Sensitivity tests showed that out of 90 strains of staphylococci from impetiginous lesions, 64 (71%) were resistant to penicillin and of these, 54 (84%) were of Type 71.

Streptococcus pyogenes was found in pure culture in 6 cases, and together with *Staph. aureus* in 12 cases. In most of the mixed cases it appeared to be a secondary invader, since its incidence increased with the age of the lesion. It was noted that staphylococci of Type 71 were never found along with streptococci of the agglutination pattern 3/13/B3264. Attempts to isolate a virus connected with the impetigo in 20 cases were unsuccessful, and it is thought that a previously reported association of impetigo with the virus of herpes simplex was probably coincidental.

Epidemiological studies were not conclusive, but over 90% of patients with a known contact with impetigo yielded *Staph. aureus* of Type 71, compared with 65% of those without a definite known contact. The nasal carriage rate of the organism among cases of impetigo was considered to be too low for this to be important epidemiologically. Treatment with aureomycin or neomycin was rapidly successful in all but 7 of the cases. *E. H. Johnson*

203. **Experimental Investigations on Mechanism Producing Acute Dermatophytosis of Feet**

R. L. BAER, S. A. ROSENTHAL, J. Z. LITT, and H. ROGACHEFSKY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 184–190, Jan. 21, 1956. 16 refs.

In the study here reported from New York University Post-Graduate Medical School, volunteer subjects exposed themselves by immersing the right foot for 30 minutes in a basin of water that had been contaminated either by the previous immersion of a foot with proved fungous disease or by the addition of fungus culture material. Other volunteers whose feet carried one type of fungus exposed a foot to water contaminated with another type of fungus.

Among 68 uninfected subjects not a single instance of clinical fungus disease was noted, despite the fact that fungal mycelia were found, at the twice-weekly microscopical and cultural examination of feet scrapings, on one or both feet of 37 (54·4%) during the 6 weeks after exposure. In 19 cases the exposed foot was involved, in 5 the other (control) foot, and in 13 both feet. In the second experiment superinfection was achieved in 4 of 20 fungus-infected persons. In one instance *Trichophyton rubrum* was induced to grow where *T. mentagrophytes* had existed before, and in 3 instances the reverse was achieved. All were asymptomatic infections.

The authors consider that the resistance of the patient, rather than exposure to infection, is the more important factor in the aetiology of fungus infections of the feet, and suggest that public and individual measures against these infections should be based on the maintenance of local resistance rather than on measures designed to prevent infection. *R. R. Willcox*

Paediatrics

204. **Leprechaunism**
P. R. EVANS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 479–483, Dec., 1955. 5 figs., 10 refs.

The term "leprechaunism" was introduced by Donohue in 1948 to describe a clinical syndrome in children, characterized by "elfin" facies, retarded development, enlargement of the nipples, cystic ovaries, and enlargement of the clitoris and labia minora, which he had observed in 2 sisters. In the present paper the author describes 2 further examples and suggests that the cause may be anomalous anatomical development with foetal ovarian hypersecretion.

Wilfrid Gaisford

PREMATURITY AND NEONATAL DISORDERS

205. **A Controlled Clinical Trial of Effects of Water Mist on Obstructive Respiratory Signs, Death Rate and Necropsy Findings among Premature Infants**
W. A. SILVERMAN and D. H. ANDERSEN. *Pediatrics* [*Pediatrics*] **17**, 1–10, Jan., 1956. 4 figs., 6 refs.

A controlled clinical trial was designed to study the effects of nebulized water mist as compared with standard operating conditions (90 to 100% relative humidity) upon respiratory symptoms, death rate, and necropsy findings among premature infants in the first 72 hours of life. In the premature nursery of the Babies Hospital, New York, 200 infants were studied over a 10-month period of time. There was no practical beneficial effect that could be credited to nebulized water-mist therapy of these infants.—[From the authors' summary.]

206. **Kernicterus and Prematurity**
V. M. CROSSE, T. C. MEYER, and J. W. GERRARD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 501–508, Dec., 1955. 1 fig., 14 refs.

Kernicterus as a hazard of prematurity has been recognized since 1950. In the study here reported from the Sorrento Maternity Hospital, Birmingham, 60 premature infants who developed kernicterus were compared with 60 "normal" premature infants and also with all premature infants (2,608) admitted during the period of study (1951–4). The mortality among all premature infants admitted was 25·6%, among the controls 17%, and among those with kernicterus 73%. Of the affected infants, only 16 survived the neonatal period; 3 of these died before the age of one year and 3 were lost to follow-up, while the remaining 10 are all retarded in speech and mentality, and in only one is the hearing unimpaired. The incidence of kernicterus and the mortality decreased as the birth weight rose.

Such factors as birth order, sex, multiple births, and complications of pregnancy were all analysed for a possible bearing on the aetiology, but with little positive result. Of the post-natal factors examined (which included the period of starvation and the amount of oxygen and sedatives given), the dosage of vitamin K appeared to be the most significant. For example, only 2 infants in the control group received more than 50 mg. of vitamin K, compared with 13 in the affected group; the indications for administration of the vitamin were haemorrhagic diathesis (9 cases), suspected intracranial haemorrhage (2), and delay in the introduction of feeds (2). A survey of the dose of vitamin K and the incidence of kernicterus for the years 1945–54 showed there was a positive correlation between the two. The mechanism is discussed, with reference to the possible haemolytic and "toxic" properties of vitamin K. A study of the serum bilirubin level carried out on 12 of the affected infants showed that in 10 of them it rose above 18 mg. per 100 ml. Later work has not, however, borne out this observation, for 6 premature infants with serum bilirubin levels above 18 mg. per 100 ml. did not develop kernicterus. The role of anoxia as a predisposing factor, occurring either during or before delivery, is also discussed. The authors conclude that hepatic immaturity probably plays the most important role in the development of kernicterus, owing to the inability of the liver of the premature infant to clear the blood of the indirect-reacting bilirubin; substitution therapy with a suitable liver extract might be helpful, but until such a substance is found exchange transfusion appears to offer the best hope whenever the serum bilirubin content threatens to reach a dangerously high level.

David Morris

207. **Hypoprothrombinaemia in the Newborn**
A. S. DOUGLAS and P. DAVIES. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 509–512, Dec., 1955. 4 figs., 13 refs.

It is now known that the finding of a prolonged blood-clotting time by Quick's one-stage test may be due to a deficiency not only of prothrombin but also of the coagulation Factors V and VII. At the United Oxford Hospitals the authors have therefore determined the content of prothrombin, Factor V, the precursor of prothrombin, and Factor VII, the main factor responsible for the prolongation of the one-stage "prothrombin" time, in the blood of 42 newborn infants. Blood was taken soon after birth from the umbilical vein (by venepuncture to avoid clotting) and again at 48 to 72 hours from the antecubital or jugular vein. Half of the infants were given 10 mg. of "synkavit" (water-soluble vitamin K) at the time the cord blood was taken. Prothrombin was estimated by the two-stage area method of Biggs and Douglas (*J. clin. Path.*, 1953, **6**, 15), Factor V by the activation of "purified" prothrombin and by the ability to correct stored normal oxalated plasma,

and Factor VII by the method of Biggs and MacFarlane. It was found that the values for prothrombin and Factor VII were both at a reduced level in the cord blood and that these levels fell considerably on the third day. In the infants given synkavit the level on the third day had risen to that present at birth, but no higher. The authors therefore conclude that the "hypoprothrombinaemia" of the newborn is due to a deficiency of Factor VII and prothrombin, that of Factor VII being the more important. The clinical correlation of these results with haemorrhagic disease of the newborn is discussed. Attention is drawn to other possible factors, such as the thrombin–fibrinogen reaction and the inability to form intrinsic thromboplastin, which may account for the failure of vitamin K to control the haemorrhagic manifestations of the disease.

David Morris

208. **Potassium Levels in Exchange Transfusion**
W. A. B. CAMPBELL. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 513–516, Dec., 1955. 2 figs., 6 refs.

The sudden and unexpected death at the Royal Maternity Hospital, Belfast, of 2 infants during exchange transfusion for relatively mild haemolytic disease of the newborn led the author to study the serum potassium level in 20 infants receiving 21 exchange transfusions, specimens of cord blood being taken for this purpose at the beginning of the transfusion and after each 100 ml. of the exchange. In all, 104 samples were examined, and in 13 of these the potassium concentration was 28 mg. per 100 ml. or above. There were 4 deaths in this group and in 3 of these cases the potassium level was above 32 mg. per 100 ml. No correlation was found between these values and the potassium level in the bottle of blood used. On the assumption that glucose and insulin remove potassium from the extracellular to the intracellular fluid, 16 infants received 2 units of insulin into the umbilical vein after the first 100 ml. of the exchange transfusion had been given; (glucose was abandoned as it made the syringe sticky, thus adding to the technical difficulties). The potassium levels in the infants so treated tended to be lower than those in the previous group; there was only one death in this group—that of a 6-lb. (2·7-kg.) infant with very intense jaundice, death occurring during a second transfusion.

The author emphasizes that no definite conclusions can be drawn from these preliminary observations but he considers that they justify further investigation.

David Morris

209. **Haemolytic Disease of the Newborn as a Family Problem**
W. WALKER and S. MURRAY. *British Medical Journal* [*Brit. med. J.*] **1**, 187–193, Jan. 28, 1956. 2 figs., 21 refs.

Observations on 1,336 pregnancies in 1,033 families during the 8-year period 1947–55 provided the material for a study of the pattern of haemolytic disease of the newborn in successive pregnancies in affected families. Serological was preferred to clinical evidence for the diagnosis of haemolytic disease, the criteria used being defined and a new system of classification of degrees of severity introduced. The haemoglobin content of cord blood is regarded as the most reliable single index of severity. The incidence of haemolytic disease during the preceding 4 years in the counties of Northumberland and Durham had been 5 cases per 1,000 births.

In 74 cases in which the mother was presumed to have been immunized by transfusion of Rh-positive blood there was no evidence of an increased risk of stillbirth, although there was some evidence that the severity of the disease in liveborn babies was increased in such cases. The first affected baby was studied in 853 cases, in 6% of which the infant was stillborn. Of the liveborn, 57% required treatment. It was clear, therefore, that there was no support for the opinion that the disease is mild in the first affected baby in a family. Where previous babies had been affected there was a tendency towards increased severity in the second affected baby, but mild disease in the firstborn was very often followed by mild disease in the second, whereas a stillbirth followed a severely affected baby in 20% of cases. When the firstborn was mildly affected the next baby also survived without treatment in 60% of cases. If the firstborn was seriously affected, the next liveborn child was severely affected in 60% of cases. The risk of intra-uterine death was 70% after one previous stillbirth and 80% after more than one stillbirth. A history of kernicterus in a previous baby almost always meant that the next baby would require exchange transfusion, but with this treatment the prognosis for the baby was excellent. There was some evidence of an increased risk of severe disease if immunization occurred early in pregnancy, but once a woman was immunized, the length of the interval between pregnancies made no difference to the prognosis.

Consideration of the family pattern gave little help in prognosis, although it was noted that where there had been a similar outcome in two pregnancies a repetition of that outcome was likely in any subsequent pregnancy and that a spontaneous live birth rarely followed a stillbirth or the birth of a severely affected baby.

John Murray

210. **The Prophylaxis of Ophthalmia Neonatorum with Quaternary Ammonium Compounds.** (Die Prophylaxe der Neugeborenenblennorrhoe mit quartären Ammoniumverbindungen)
R. SIEBECK and E. WALCH. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 70–72, Jan. 13, 1956. 1 fig., 24 refs.

Writing from the University of Heidelberg the authors first list the common objections to the routine use of silver nitrate as a prophylactic against ophthalmia neonatorum; in their view the sulphonamides are also ruled out because of the increasing incidence of resistant strains of gonococci, while penicillin appears unsuitable for various reasons. However, a non-irritant substance with a wide antibacterial spectrum, which is stable on storage, diffuses readily, and is free from the disadvantages of antibiotics, was found among the quaternary ammonium compounds. The substance used, "quartamon", has been successfully employed in a series of 1,875 intraocular operations as an anti-infective agent.

Its antibacterial action was tested by a tube method in concentrations of 0·01, 0·05, 0·1, and 0·5% against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and gonococci, and also by a disk method with subcultures from the zones of growth inhibition. Concentrations above 0·05% were 100% effective against gonococci; it was also shown that up to 5 minutes after instillation of a 0·5% solution of quartamon into the conjunctival sac of the rabbit a bactericidal concentration of the compound was maintained. No irritant effect was noted.

On the strength of these tests one drop of quartamon in the 0·5% solution was instilled into each eye of 100 newborn babies and 24 hours later a swab was taken from both eyes. Irritant effects such as lacrimation and mild conjunctival reddening occurred in 8 cases, while 10 of the infants showed a mild conjunctival leucocytosis—compared with the usual 20% of those treated with silver nitrate. Pathogenic organisms were identified in 4 cases; one mild case of ophthalmia was due to a haemolytic staphylococcus. Subsequently quartamon was used in a further series of 250 newborn infants. Mild irritation was noted in 12 cases and organisms were found in 6; 2 cases of non-gonococcal ophthalmia occurred. In one case the mother of a healthy baby was found to suffer from active gonorrhoea: yet the baby remained free from infection although only a single drop of quartamon had been instilled.

F. Hillman

211. **Myocarditis in the Newborn Infant. A Study of an Outbreak Associated with Coxsackie Group B Virus Infection in a Maternity Home in Johannesburg**

S. N. JAVETT, S. HEYMANN, B. MUNDEL, W. J. PEPLER, H. I. LURIE, J. GEAR, V. MEASROCH, and Z. KIRSCH. *Journal of Pediatrics* [*J. Pediat.*] **48**, 1–22, Jan., 1956. 14 figs., 6 refs.

The clinical features of an infection occurring in 10 infants born during a 3-week period in October and November, 1952, at a maternity home in Johannesburg are described. The ages of the infants at onset of the illness ranged from 5 to 17 days. In most of them there was an initial phase of malaise with a few loose stools followed by apparent recovery; 3 to 8 days later, when the second phase started, the picture was that of a fulminating infection with circulatory collapse. Within 24 hours of the onset of the acute phase 6 infants died, and post-mortem examination, which was carried out on 3 of them, revealed patchy myocarditis as the outstanding lesion; in one case there was also patchy encephalitis. The results of bacteriological investigations were negative. However, Coxsackie Group-B virus was isolated from the stool of one infant who recovered, and baby mice inoculated with a suspension of brain from 2 of the infants who died developed lesions resembling those produced by Coxsackie Group-B virus.

In an additional note to the paper the authors state that this virus has since been isolated from the heart muscle of a newborn infant dying from myocarditis (some time after the above outbreak) and that details of this case are to be published.

Margaret D. Baber

212. **Rectal Temperatures of Term Newborn Infants with Apnea**

J. H. MCCLURE and W. L. CATON. *Journal of Pediatrics* [*J. Pediat.*] **48**, 23–27, Jan., 1956. 4 figs., 2 refs.

The authors report, from Emory University School of Medicine, Atlanta, Georgia, the chance observation of the occurrence of a considerable rise in the rectal temperature of 4 newborn infants during the period of apnoea immediately following delivery. All 4 were full-term infants, 3 being delivered vaginally and one by Caesarean section, and there was no common factor in the maternal history or type of anaesthesia or sedation that might have accounted for the apnoea. The rectal temperature, which was recorded continuously with the thermistor element of a telethermometer, rose as much as 2·5° F. (1·4° C.) during the period of apnoea and fell precipitously by 1·3° F. (0·72° C.) in 30 seconds from the onset of respiration. [The temperature range is best appreciated by examination of the graphs in the original article.]

[This report stimulates speculation on the possible physiological explanation of the authors' findings and should lead to further work in this field.]

David Morris

CLINICAL PAEDIATRICS

213. **The Periodic Syndrome**

J. J. KEMPTON. *British Medical Journal* [*Brit. med. J.*] **1**, 83–86, Jan. 14, 1956. 23 refs.

In some children a syndrome of which the main features are headache, pallor, abdominal pain, vomiting, and pyrexia, or any combination of these, tends to recur with a certain rhythmic regularity, though in others the intervals between attacks are quite irregular. There are other, less common, manifestations of this disorder, such as sensory disturbances or temporary alteration of bowel habit, but there are no physical signs of organic disease. This condition has been known for over 70 years and many names have been proposed for it—for example, cyclical vomiting—but the aetiology remains largely unknown. The author suggests that the term "periodic syndrome" covers all types of case without necessarily implying a common or known aetiology.

Among a number of causative factors the main ones appear to be a familial tendency, a focus of upper respiratory infection, and a nervous element. It has been suggested that progressive biochemical changes occur, resulting in depletion of liver glycogen, and that these might be attributed to oversecretion of adrenaline setting up a vicious circle which would account for all the common clinical features. The appearance of ketones in the breath and the urine is related simply to the depletion of liver glycogen, and the disturbance of fat metabolism is now regarded as purely incidental. Aspirin and sweetened fluids are often effective in treatment.

The differential diagnosis is discussed, with a warning that other, more serious, illnesses may be missed in a child who is subject to the periodic syndrome.

John Lorber

214. **Non-endocrine Dwarfism and Pseudoepiphyses**
R. WAGNER. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 6–13, Jan., 1956. 6 figs., 7 refs.

A syndrome characterized by dwarfism, retarded bony development, and a congenital heart murmur was observed in 11 children (10 males and 1 female); all except 2 also showed pseudo-epiphyses, most often at the proximal end of the second metacarpal bones. Sexual infantilism was present in 3 of the patients who were over 13 years of age. A systolic murmur was heard along the left border of the sternum, loudest at the third intercostal space. None of the patients had cyanosis or clubbing of the fingers. The author considers that the heart lesion was probably an interatrial or interventricular septal defect, but no special investigations were carried out to determine the diagnosis. Mental development was in most instances normal, severe mental retardation being present in only one case.

It is suggested that the syndrome is genetically determined; none of the patients, however, were related to each other or, apparently, had any affected relatives.

C. O. Carter

215. **Sudden Mental Deterioration with Convulsions in Infancy**
R. S. ILLINGWORTH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 529–537, Dec., 1955. 7 figs., 4 refs.

Mental changes in infancy are associated with a variety of conditions, often regarded as causative. The present author, from his experience at the Children's Hospital, Sheffield, considers that in one group of children fits and mental deterioration develop simultaneously after a period of normal development, while in another group, also previously normal, fits are followed months or years later by mental decay. He describes 12 cases falling into the former group.

The age at onset of the illness was 4 to 8 months. In 8 infants fits were the first abnormality noted, although in the other 4 there were vague premonitory symptoms. All the infants suddenly lost interest in their surroundings, ceased to laugh or smile, and became apathetic and dull. Neurological examination was negative, but the electroencephalogram was grossly abnormal, showing generalized paroxysmal slow activity. In all cases there was a slow improvement in the dysrhythmia with age (7 of the patients at the age of 4½ years showed mild dysrhythmia with occasional short bursts of generalized slow waves). Drugs did not completely control the fits, of which several occurred each day for some months; in 8 cases akinetic seizures, the so-called salaam convulsions, developed.

The prognosis as regards mental age is poor; in 10 of these patients the I.Q. was too low to be assessed, one had an I.Q. of 60, and in one the I.Q. had not been finally assessed. The author emphasizes the lack of parallelism between the relatively normal motor and manipulative development and the defective social responses in 8 of the children seen within 2 months of onset. This observation is of importance in prognosis.

The aetiology of the condition is not known, but the author has not observed this sequence of events in any child known to have sustained a birth injury, although this factor cannot altogether be ruled out.

J. G. Jamieson

216. **Studies in Maternal Deprivation in Infants' Homes.** [In English]
G. KLACKENBERG. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **45**, 1–12, Jan., 1956. 4 refs.

In view of the recent work by Spitz and others on emotional deprivation in infancy the author set out to determine the psychological effect of separation from the mother on 100 babies in infants' homes run or supervised by the Stockholm Board of Social Welfare. These children were divided into two groups of 50: (1) those who had been admitted at an age of less than one month and had been in the home up to approximately one year of age; (2) those who had been cared for by their own mothers until the age of 6 months or more, when they entered an institution. The controls (Group 3) consisted of 21 foster children who, from the first month up to one year of age, had been looked after in their prospective adoptive homes. The composition of the groups in respect of the social origin of the children was the same, all classes being represented, with the lowest predominating. All the babies were subjected to a Bühler–Hetzer test, examined physically, and observed at play between the ages of 9 and 12 months.

The mean Bühler–Hetzer quotient for Group 3 was significantly higher than those for Groups 1 and 2, between which there was no appreciable difference. Ten of the 100 children in Groups 1 and 2 could not be tested because of difficult behaviour, while all the children in Group 3 were cooperative in the tests. Emotional stability was lowest in Group 2. There was only one possible case of severe anaclitic depression. The emotional and mental atmosphere in the infants' homes was very good, and the number of children per nurse was never more than 3. *R. S. Illingworth*

217. **The Weight in Pink Disease**
T. COLVER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 524–528, Dec., 1955. 1 fig., 3 refs.

Weight trends in pink disease are not described in the literature, but they merit attention because they are the only serial observations which are strictly objective, easily determined, and uninfluenced by unfamiliar surroundings in clinic or hospital. Observations in 100 cases of pink disease at the Children's Hospital, Sheffield, are reviewed. The average duration of the disease was 17 weeks, but 2 patients died in the fourth and twelfth weeks respectively. In 13 of the infants no loss of weight was observed, while in 11 there was a loss of 11% or more. Three features were common to all of the infants in the latter group: (1) an appreciable interval had elapsed between the onset of symptoms and the first visit to hospital; (2) the weight loss occurred in one uninterrupted stage; and (3) this stage occurred during the early part of the observation period. The author considers that in those cases in which weight was unchanged

the loss had actually taken place before the patient was brought to hospital, a view supported by the number of children seen a few weeks after the onset who continued to lose weight for a short time and then began to gain weight.

Discussing the weight curve in relation to clinical progress, the author states that during the period of weight loss there was an increase in symptoms; then came an abrupt change, which was noticed by the mother even if it was not revealed in the infant's appearance. This " turn " appeared to coincide roughly with a period in which weight was stationary; in nearly all cases, unless there was intercurrent infection, recovery and weight gain then continued without interruption. It is emphasized that since there is always delay before the infant is seen in hospital, improvement is to be expected, on the average, one week after the first visit—an important point in the evaluation of treatment of pink disease.

J. G. Jamieson

218. **Severe Type of Infantile Hypercalcaemia**
B. E. SCHLESINGER, N. R. BUTLER, and J. A. BLACK. *British Medical Journal* [*Brit. med. J.*] **1**, 127–134, Jan. 21, 1956. 5 figs., 26 refs.

The recently recognized condition of infantile hypercalcaemia occurs in both a benign and a severe form. In this paper from the Hospital for Sick Children, Great Ormond Street, London, the authors review 7 published cases of the severe form and add 3 new cases, all in infants under 2½ years of age. The patients present a characteristic elfin facies and often have a convergent squint; they resemble cretins but are hyperkinetic, and in all survivors so far mentality has been retarded. The skull is always small and occasionally craniostenotic. In the acute stage growth is slowed or stopped, but is resumed when hypercalcaemia ceases, although the patients remain small in stature. The degree of hypercalcaemia is similar to that in the benign form, but is of longer duration; azotaemia is invariable, cellular deposits in the urine being frequent, and many patients also have a high blood cholesterol level, while a low serum alkaline-phosphatase and a rather high serum protein content may sometimes be found. A loud systolic murmur and systemic hypertension are to be expected. The bony changes seen radiologically may be severe or so slight as to be overlooked; they comprise thickening of the skull and long bones, with opaque transverse lines in the shafts of the bones, and dense irregular epiphyseal calcification. At post-mortem examination shrunken calcified kidneys, cardiac hypertrophy, valvular calcification, and the thickened bones are salient features. Renal glomerular destruction is widespread and severe, while metastatic calcification is sometimes extensive, resembling that in hypercalcaemia from known causes.

The authors, who formerly attributed the syndrome to congenital abnormalities, now believe, in the light of these further post-mortem studies, that the prolonged hypercalcaemia and renal impairment can be held to account for most of the signs and symptoms, and possibly also for the mental defect, although some of the patients seemed to be retarded at the onset of the illness. The hypercholesterolaemia may also be concerned with renal damage, but the facial changes are difficult to explain; hypersensitivity to normal doses of vitamin D is an aetiological hypothesis. Treatment consists in providing a low calcium diet, perhaps with the addition of cortisone. Most of the differences between the benign and severe types can be explained on the assumption that in the severe type derangement of calcium metabolism begins earlier and is of greater degree. *M. E. MacGregor*

219. **The Intestinal Absorption of Carbon-labelled Oleic Acid in the Normal Infant and in Congenital Bile Duct Atresia.** [In English]
R. BLOMSTRAND and B. LINDQUIST. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **10**, 627–639, Dec., 1955. 3 figs., 34 refs.

At the Paediatric Clinic of the University of Lund intestinal fat absorption was studied in 2 normal infants and one child with congenital atresia of the bile ducts by means of oleic acid labelled with radioactive carbon (^{13}C). It was shown that the major part of the faecal fat in all 3 subjects was unabsorbed dietary fat, which also accounted for the steatorrhoea in the case of atresia of the bile ducts. A small amount of oleic acid appeared to have been hydrogenated in the intestinal lumen; otherwise the acid passed unchanged through the alimentary canal.

An average of 85% of the labelled oleic acid was absorbed by the two normal infants compared with 42% by the child with biliary atresia. *A. C. Frazer*

220. **The Intestinal Absorption of Carbon-labelled Oleic and Palmitic Acid in the Normal Infant and in Cystic Fibrosis of the Pancreas.** [In English]
R. BLOMSTRAND, B. LINDQUIST, and K. PÄÄBO. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **10**, 640–648, Dec., 1955. 2 figs., 11 refs.

Intestinal absorption of fat was studied in a healthy child and in a child with fibrocystic disease of the pancreas by means of oleic and palmitic acids, labelled with radioactive carbon (^{13}C) and incorporated into glycerides. Most of the faecal fat in both these subjects was shown to be derived from unabsorbed dietary fat, although a significant contribution from non-dietary sources was observed, which was greater in the child with pancreatic fibrosis than in the normal child. A small amount of the oleic acid was hydrogenated in the intestinal lumen.

A. C. Frazer

221. **Oesophageal " Spasm " in Infancy**
R. ASTLEY. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 1045–1049, Dec., 1955. 5 figs., 8 refs.

In infancy, temporary obstruction of the oesophagus just above the diaphragm, either complete or partial, is usually associated with gastro-oesophageal incompetence and a small loculus of intrathoracic stomach. Clinically there is vomiting after food, which begins soon after birth. On radiological examination after a barium meal there is obstruction of the oesophagus 2 or 3 centimetres

above the diaphragm; below this the barium passes as an intermittent jet or trickle through an irregularly-narrowed lumen. However, once enough barium has passed through, compression of the abdomen fills this narrow passage and makes it balloon out to a greater width than the rest of the oesophagus, showing it to be an intrathoracic segment of stomach. From follow-up studies of infants with an intrathoracic cardia it appears that the obstructive element of the condition gradually subsides but the incompetence remains, although it does not cause symptoms. The only treatment is by nursing in the upright position.

In one case reported from the Children's Hospital, Birmingham, there was oesophageal obstruction with at the same time intense peristaltic activity; this followed removal of an intrathoracic cyst and was probably due to damage to the vagus nerves. *Marianna Clark*

222. **Infantile Pyloric Stenosis**
J. W. GERRARD, J. A. H. WATERHOUSE, and D. G. MAURICE. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 493–496, Dec., 1955. 1 fig., 6 refs.

In an attempt to assess the influence of postnatal environment on the development of infantile pyloric stenosis the authors first measured the length and diameter of the pyloric tumour at operation in 51 cases treated at the Children's Hospital, Birmingham. They confirmed that the size was closely related to the age of the infant and to the duration of the signs.

They next considered the influence of different feeding schedules on the development of the condition in these 51 cases and 10 others selected at random from the hospital files. They found that in infants who had been fed 3-hourly the signs developed at a significantly earlier date than in those who had been fed 4-hourly (21·6 days as against 27·1). Infants born in hospital tended to develop signs of pyloric stenosis later than those born at home, which may be attributable to the fact that 4-hourly feeding schedules are more common in hospital and 3-hourly at home.

Analysis of the 152 cases according to birth rank and comparison with the distribution of birth rank in Birmingham as a whole during the same period showed no increased incidence of pyloric stenosis in firstborn children. *Wilfrid Gaisford*

223. **Studies of Distal Colonic Motility in Children. III. The Pathologic Physiology of Congenital Megacolon (Hirschsprung's Disease)**
M. DAVIDSON, M. H. SLEISENGER, H. STEINBERG, and T. P. ALMY. *Gastroenterology* [*Gastroenterology*] **29**, 803–824, Nov., 1955. 10 figs., 37 refs.

In patients suffering from achalasia of the cardia the muscle of the lower third of the oesophagus is peculiarly sensitive to cholinergic drugs. This is thought to be an example of the general principle that denervated structures are abnormally sensitive to the chemical mediators of synaptic transmission circulating in the blood stream. In a study carried out at New York Hospital–Cornell Medical Center, New York, the authors endeavoured to show that a similar phenomenon occurs in the case of Hirschsprung's disease. The method of investigation consisted in introducing three open-ended, pressure-recording catheters into the rectum and lower colon of 20 normal subjects and 6 patients with megacolon.

Of the healthy subjects, 9 showed diminution in contractile activity of the bowel after the injection of methacholine chloride in doses sufficient to produce lacrimation, but in the remaining 11 there was no change in bowel motility. In 2 of the 6 patients with megacolon the lower bowel showed no response at all to methacholine, while in a further 2 the colon above the aganglionic segment relaxed, but motility in the obstructing region was unaffected; operation in these 4 cases revealed the classic pathological changes of Hirschsprung's disease. In the fifth case the bowel was shown to relax above the obstructing segment, but the patient refused operation. In the sixth case only the lower part of the rectal ampulla failed to relax under methacholine stimulation. This case had not been diagnosed as one of Hirschsprung's disease because barium enemata did not show the typical narrowed segment; in view of the results of the motility studies, however, it was decided to remove the unresponsive part of the rectum. Despite the fact that the resected bowel contained normal ganglion cells throughout, the patient was clinically cured.

The authors conclude that the aganglionic segment of the colon is not hypersensitive to cholinergic drugs because, unlike achalasia, Hirschsprung's disease is a congenital abnormality. They suggest that pressure recordings may help occasionally to clinch the diagnosis in difficult or borderline cases, such as that of their sixth patient. *A. G. Parks*

224. **Paroxysmal Tachycardia in Infancy**
J. APLEY, B. D. CORNER, and T. C. GIBSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 517–523, Dec., 1955. 4 figs., 22 refs.

In this paper from the University of Bristol and Bath Royal United Hospital the clinical picture in 13 cases of paroxysmal tachycardia in early infancy is discussed and 3 fatal cases are described in detail. Generally, the patient appeared listless, was unwilling to feed, and was often feverish and restless. In 4 cases the temperature rose, this being due to pneumonia in 2 and cardiac failure in 2. The most obvious symptom in all cases was respiratory disturbance with rapid, laboured breathing. In half the cases radiological examination indicated some congestion of the lung. Slight cyanosis was present in 8, while in 11 the liver was greatly enlarged. Clinically, it was difficult to ascertain the size of the heart, which was determined accurately in only 2 cases. Enlargement of the heart was, however, diagnosed radiologically in 3 cases. The pulse rate, which was very rapid, was best estimated by auscultation of the heart, but in one case this estimation was very inaccurate because of the presence of pulsus alternans. In 12 cases the electrocardiogram (ECG) was recorded during an attack. Pulse rates varied from 210 to 290 per minute, tachycardia being apparently supraventricular. Auricular flutter was observed in only one case. During

periods of normal rhythm the ECG was normal in all but one case, in which exceptionally tall P waves were noted immediately after an attack. In the one case in which a tracing was not obtained during an attack the ECG during normal rhythm suggested that there was a left bundle-branch block due to premature activation of the right ventricle.

In the authors' view, mechanical methods of inducing vagal stimulation are unsatisfactory in treatment. Administration of digoxin, with the object of combating failure rather than of controlling the tachycardia, seemed to be of value and was well tolerated. The patients were nursed in oxygen tents and received chloral hydrate when sedation was needed. Digitalis was given prophylactically for 6 months after the first attack, but the efficacy of this measure has not yet been assessed.

In 9 cases in the series the cause of the condition was not found; in 2 there was pulmonary infection, in one case necropsy revealed interstitial myocarditis, and in the remaining case there was endomyocardial fibroelastosis. The prognosis appears to improve with age, the danger in early infancy being acute failure, which may prove fatal. The authors state that it was exceptional for further attacks of tachycardia to occur more than 6 months after the initial illness.

J. G. Jamieson

225. **Coarctation of the Aorta with Congestive Heart Failure in Infancy—Medical Treatment**
H. T. LANG and A. S. NADAS. *Pediatrics* [*Pediatrics*] 17, 45–57, Jan., 1956. 14 figs., 23 refs.

The optimum age for operation for coarctation of the aorta is stated to be between 8 and 20 years. However, in some infants with this lesion congestive heart failure has developed, and this has led to a number of attempts to relieve the aortic block within the first few months of life. The authors of this paper from the Children's Medical Center, Boston, discuss the medical management of 9 cases of coarctation of the aorta with congestive heart failure in infancy, in all of which there were signs of both left- and right-sided failure. There was generalized cardiomegaly with pulmonary congestion, and the infants over 6 months of age showed left ventricular hypertrophy. Medical treatment, consisting in administration of digitalis, oxygen, diuretics, antibiotics, and a low-sodium diet, was successful, operation being safely postponed in every case.

It is concluded that in the majority of cases such medical treatment can be given until the optimum age for surgical intervention, but that an operation should be performed early if medical management fails or hypertensive encephalopathy develops. *I. A. B. Cathie*

226. **Staphylococcal Pneumonia in Infancy**
I. S. WALLMAN, R. C. GODFREY, and J. R. H. WATSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1423–1427, Dec. 10, 1955. 8 figs., 10 refs.

The literature on staphylococcal pneumonia is reviewed briefly. Attention is drawn to an apparent increase in frequency of the disease and its high mortality.

A series of 55 cases in children under the age of 2 years, occurring during a period of 29 months, are discussed. Eleven of them were associated with chronic debilitating disease, the pneumonia being a terminal event (Group A). The remaining 44 cases (Group B) are discussed in detail with reference to diagnosis, *x*-ray changes, treatment, and prognosis. Ten patients died—a mortality of 23%.

The relative ineffectiveness of the broad-spectrum antibiotics in controlling the infection is stressed, and the high percentage of penicillin-resistant organisms is noted (92%). Empyema or pneumothorax was present in 28 cases (64%). Emphasis is laid on the importance of surgical treatment when these complications occur. Cysts were present in 29 cases (66%). Follow-up *x*-ray examinations in 29 out of the 34 survivors showed nothing abnormal, there being no residual signs or symptoms.—[Authors' summary.]

227. **The Virus Aetiology of Interstitial Pneumonia in Infants.** (Über die Virusätiologie der interstitiellen Säuglingspneumonie)
L. MOSER. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] 77, 349–362, 1955. 2 figs., 48 refs.

The discovery by Vaněk and Jírovéc in 1952 of characteristic parasites (to which the name *Pneumocystis carinii* has been given) in the lungs of infants dying of interstitial plasma-cell pneumonia has since been amply confirmed. Some difference of opinion still exists as to whether these organisms are protozoa or yeasts, but it is generally assumed that they are causative, and the theory of a virus aetiology, previously favoured by many, has been abandoned. This theory was in fact based largely on the repeated failure to isolate any micro-organism despite the obviously infective nature of the disease.

The present author now reports the results of serological investigations carried out at the Institute of Hygiene, Hamburg, which in his opinion favour a virus aetiology. By centrifuging homogenized lung tissue from cases of interstitial plasma-cell pneumonia suspended in bovine albumin solution (10 minutes at 300 r.p.m., followed by 30 minutes at 3,000 r.p.m.) he obtained four layers, of which the most superficial contained masses of minute granules which stained red with Giemsa's stain and which the author considered to be viral elementary bodies. From this layer an antigen was prepared and tested by means of a complement-fixation reaction. The serum of all infants with interstitial plasma-cell pneumonia gave positive reactions up to a titre of 1 : 512, whereas that of all other infants tested gave negative reactions. Out of 582 sera from adults, 552 gave negative reactions, but 6 out of 10 sera from relatives of infected infants and 18 out of 105 from members of the nursing staff gave positive reactions. Serological evidence is presented which suggests that occasional intra-uterine transmission takes place.

[The antigen prepared by the author appears to be potent and specific and should therefore be of great value in diagnosis and in the differentiation of carriers. However, he has not excluded the possibility that the granules are cytoplasmic or nuclear fragments of a larger parasite, and in view of this the results of the serological tests cannot be regarded as conclusive evidence of a virus aetiology.] *H. S. Baar*

228. **The Aetiology of Interstitial Plasma-cell Pneumonia (Saccharomycosis) in Infancy.** (Zur Ätiologie der interstitiellen plasmocellulären Pneumonie (Saccharomykose) im Säuglingsalter)
K. O. SCHMID. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **66**, 426–448, 1955. 7 figs., 44 refs.

In investigations carried out at the Institute of Pathology of the University of Graz on necropsy material from 8 infants who died of interstitial plasma-cell pneumonia haematogenous spread of the infection was proved by the demonstration of typical parasites in a branch of the pulmonary artery. Bacteriological investigations, with animal inoculation, were carried out in one case; whereas the animal inoculations gave negative results, cultures yielded growth of *Saccharomyces fragilis*. *Candida albicans*, and *Candida krusei*. In cultures of *Saccharomyces fragilis* forms were found which were regarded as identical with the foamy and honey-combed structures seen in histological sections and in imprints of the lungs in cases of interstitial plasma-cell pneumonia. Moreover, Gram-negative forms of the yeast were present in the cultures, so that, in the author's opinion, the Gram-negative nature of the infecting organism found in the lungs cannot be regarded as conclusive evidence that the organism is a protozoon. In glucose–broth cultures of the yeast "eight-granule forms", indistinguishable from those seen in lung-imprints, were noted. The author considers the foam-structures typically found in the lung to be the result of hydrolysis of yeast cells, which swell, become vacuolized, and finally dissolve. The conspicuous granules are considered to be intra- and extracellular ascospores.

After a discussion of his own findings and those reported in the literature the author rejects the hypothesis of the protozoal nature of *Pneumocystis carinii* and favours a *Saccharomyces* as the causative organism of interstitial plasma-cell pneumonia, for which he proposes the term "saccharomycosis". He considers aspiration of milk to be the main source of infection.

H. S. Baar

229. **Primary Enuresis. When is a Child Dry at Night?** [In English]
G. KLACKENBERG. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 513–518, Nov., 1955. 1 fig., 2 refs.

A study was made of 315 normal children (48·6% male, 51·4% female) attending a Child Welfare Centre in Stockholm to determine at what age they became habitually dry at night. In 7·9% of cases the child was already dry at night at the age of one year, 60% were dry at 2 years, and 87% when they were 3 years old, while at 6 years only 4% were still habitually wet at night, this being regarded as "physiological" wetting, although in some cases it may have been prolonged by emotional conflicts. That the development of urinary control at night is a process of maturation of the nervous system and is not the result of training is shown by the fact that the age at which it is accomplished bears no relation to the age at which such training began or the regularity with which it is carried out. Indeed, the author stresses the danger of too coercive and rigid a form of "cleanliness training" in causing or perpetuating lack of control in a child who actively resents being woken at night and held on a pot.

Winston Turner

230. **Wilms's Tumour: its Treatment and Prognosis**
L. S. SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 200–203, Jan. 28, 1956. 3 figs., 27 refs.

To determine the factors which influence the results of treatment of Wilms's tumour and the prognosis in this condition, 61 cases seen at the Royal Hospital for Sick Children, Glasgow, and 1,141 reported in the literature are reviewed. The survival rates in the latter (survival for 2 years or more) were as follows: with surgery alone, 18·8%; radiotherapy alone, 11%; preoperative irradiation and nephrectomy, 25·9%; nephrectomy with postoperative irradiation, 23·9%; and nephrectomy with irradiation both before and after operation, 31·8%. The author states that nephrectomy should be performed transperitoneally through a large abdominal or thoracic incision to allow early ligation of the renal pedicle, thus preventing the dissemination of tumour cells into the inferior vena cava during handling of the kidney. The advantage of preoperative irradiation is that the size of the tumour is greatly reduced thereby, making subsequent nephrectomy easier. A tumour which does not shrink in size after 6 to 8 exposures is radioresistant; in such cases nephrectomy should be performed without further delay. Examination of the kidneys even years after radiotherapy may reveal the presence of active epithelial cells although the connective-tissue elements have been completely destroyed—hence the need for nephrectomy. There is now general agreement, however, that a combination of nephrectomy and postoperative irradiation gives the best results. In children irradiation has little or no effect on wound healing and can therefore be given immediately after operation. They tolerate a dosage of 1,000 to 2,000 r without damage to the vertebrae, but since leucocytes appear to be vulnerable to high dosage of *x* rays the leucocyte count should be carefully watched.

Discussing prognosis, the author states that the survival rate is very much higher among patients operated on under one year of age than among those operated on later in life. In the author's series the survival rate among those treated under the age of one year was 17·6%, whereas among those over that age it was only 6·5%; the corresponding figures in the cases from the literature were 17·4 and 9·1% respectively. The prognosis is poor in the presence of haematuria, which indicates ulceration or invasion of the renal pelvis. Analysis of the age incidence in 1,000 published cases of Wilms's tumour revealed that the majority of the patients were under 4 years old.

Charles Nicholas

231. **Congenital Renal Tubular Insufficiency in Children.** (Les insuffisances congénitales du tubule rénal chez l'enfant)
R. DEBRÉ, P. ROYER, and H. LESTRADET. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 235–254, Jan. 22, 1956. 10 figs., bibliography.

Medical Genetics

232. **Heredity in Gout and Hyperuricemia.** [In English]
M. HAUGE and B. HARVALD. *Acta medica Scandinavica* [*Acta med. scand.*] **152**, 247–257, Nov. 10, 1955. 22 refs.

As a further contribution to the study of the heredity of gout and to confirm (or to refute) certain previous findings the authors determined the serum urate levels in 48 brothers and 57 sisters of 32 male patients with gout under treatment at Rigshospitalet, Copenhagen. In both sexes the mean serum urate levels were significantly greater than in a control series of subjects of the same sex and age distribution, being 6·06 and 5·05 mg. per 100 ml. for male siblings and controls respectively and 5·41 and 3·96 mg. per 100 ml. for females.

These findings confirm those of previous workers and are taken as evidence that hyperuricaemia is an inherited characteristic and predisposes to clinical gout. However, it was not found possible to draw any clear line between normal and pathological serum urate levels, and the distribution curve for these values was not consistent with the hypothesis that hyperuricaemia is determined by a single abnormal gene. The authors conclude that the control of the serum level of urates is probably under the influence of a number of different genes acting together. *H. Harris*

233. **Infantile Genetic Agranulocytosis (Agranulocytosis infantilis hereditaria). A New Recessive Lethal Disease in Man.** [In English]
R. KOSTMANN. *Acta paediatrica* [*Acta paediat. (Uppsala)*] 45, Suppl. 105, 1–78, Feb., 1956. 14 figs., bibliography.

234. **A Genetic Study of Celiac Disease. Incidence of Celiac Disease, Gastrointestinal Disorders, and Diabetes in Pedigrees of Children with Celiac Disease**
P. H. BOYER and D. H. ANDERSEN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 131–137, Feb., 1956. 11 refs.

In a genetic study of coeliac disease carried out at the Babies Hospital, New York, the index cases were 25 patients with severe coeliac disease (associated with steatorrhoea) and 25 with mild coeliac disease (with little or no steatorrhoea), who were selected from among children attending the hospital on the ground of availability of patient and parents for interview; 50 children or siblings of members of the medical and nursing staff served as controls. The information obtained was considered to be adequate and reasonably accurate.

A comparison of the relatives of the patients with the relatives of controls consistently showed among the former a higher incidence of gastro-intestinal disturbances, such as episodes of diarrhoea, urgency of defaecation after meals, and intolerance of fats. There was, however, no increase in the incidence of peptic ulcer, gall-bladder disease, or allergic diseases; in several instances the symptoms described by a patient's relative suggested that he or she had had coeliac disease. Of the 59 siblings of the index patients, 5 were considered to have severe and 9 mild coeliac disease, while 5 of the 100 parents and 5 of about 450 aunts and uncles of the patients were considered probably to have had coeliac disease. None of the siblings or other relatives of the control children were considered to have had coeliac disease. There was no significant increase in the incidence of diabetes among the children with coeliac disease as compared with the controls.

[No information is given about the comparative severity of the condition in the index case and the affected relative.] *C. O. Carter*

235. **Direct Inheritance of Alcaptonuria**
R. A. MILCH. *Metabolism* [*Metabolism*] **4**, 513–518, Nov., 1955. 16 refs.

The author points out that while many of the published pedigrees of families in which alcaptonuria appears as an inherited condition seem superficially to support a theory of inheritance by a simple autosomal recessive gene, an increasing amount of data has appeared which supports the alternative theory of inheritance by a simple dominant gene. Since most of the published pedigrees have been limited to the near descendants of affected persons, the present further study was undertaken at the Sloan-Kettering Institute, New York, on three previously reported families in which direct transmission from parent to child had been recorded, in an attempt to extend these pedigrees and, in the light of this extension, to reassess the significance of the conclusions previously reached.

All available records of the original families were examined and contact made with most of the known descendants by letter or in person. In only a few cases was physical examination possible and in only one family was an attempt made at diagnosis by chemical examination of urine. (The three families are described in detail and the family pedigrees, covering five or six generations, are shown diagrammatically.) Two families showed evidence of direct transmission of a gene with some failure of manifestation, while in the third family none of the descendants of the originally reported affected individuals was affected. In his discussion the author states that such phenomena have been reported for other conditions and appear to be best explained on the basis of an incompletely penetrant dominant gene associated with modifying genes. Such an explanation would be compatible with the pedigrees exhibited here, as also with direct transmission of the trait, the irregularities in such transmission, and the excess of affected offspring of consanguineous matings, which have all at various times been reported. *E. A. Cheeseman*

Public Health

236. **Study of Children Drinking Fluoridated and Non-fluoridated Water. Quantitative Urinary Excretion of Albumin and Formed Elements**
E. R. SCHLESINGER, D. E. OVERTON, and H. C. CHASE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 21–24, Jan. 7, 1956. 8 refs.

To determine whether long-term ingestion of water to which fluoride is added has any irritative effect on the kidneys the 12-hour urinary excretion of albumin and formed elements was studied in two groups of boys—one group of 100 living in Newburgh, New York, where the water contains fluoride and the other group, also of 100, living in Kingston, New York, where the water is essentially fluoride-free. The boys were 12 years of age, this age being selected because of the likelihood of obtaining better cooperation and because the incidence of renal disease is higher at this age than in younger children. The boys in the first group had been drinking water supplemented with fluoride for approximately 8 years. Specimens of urine were not taken if there was any history of illness during the preceding 2 weeks, but no limitation was placed on physical activity before the 12-hour specimen was taken. The method of collection and examination of the urine followed closely the technique developed by Addis and modified by Lippman.

Analysis of the findings revealed differences between the two groups which " tended to favour the Newburgh children "—that is, the group drinking fluoride-treated water—but " no medical significance can be attributed to any of the differences ". The authors consider that the study has provided additional evidence of the value in the prevention of dental caries of adding fluoride to drinking-water. *R. G. Meyer*

237. **Some Observations on London Fog**
R. E. WALLER and P. J. LAWTHER. *British Medical Journal* [*Brit. med. J.*] **2**, 1356–1358, Dec. 3, 1955. 2 figs., 4 refs.

On January 19, 1955, severe atmospheric pollution was recorded in several parts of London. The polluted air was irritant and had an odour of coal smoke, the exceptionally high concentration of which reduced visibility in certain areas to 70 yards (64 metres). The maximum concentration of smoke, measured at St. Bartholomew's Hospital, was 6·5 mg. per cubic metre, and that of sulphur dioxide 1 p.p.m. Wide variations were observed in the amount of smoke present; in fact, a tenfold increase occurred during a period of 2 hours. Sulphuric acid was not detected. Microscopical examination of samples of the suspended matter obtained with a thermal precipitator and a cascade impactor showed the presence of black smoke particles, most of which were less than 1 μ in diameter.

Daily records of their state of health made since October, 1954, by 29 chronic bronchitic and emphysematous patients attending a special clinic showed that in some instances a clinical deterioration had taken place coinciding with the change in the weather. It was difficult to form a reliable general estimate of the proportion of patients affected by the adverse atmospheric conditions; the clinical impression of physicians seeing outpatients was that these tended to cause attacks of bronchospasm and exacerbations of chronic bronchitis.

A patient with chronic bronchitis, emphysema, and cor pulmonale, who was considered to be susceptible to the effects of smog, was removed from the main ward to a room equipped with an electrostatic precipitator for removing smoke particles and a soda-lime device for reducing the concentration of acid pollutants. Tests revealed that although the smoke concentration in the main ward followed the outdoor level, the concentration in the air-conditioned room was considerably reduced (28% of the ward level). The patient remained free from any adverse reactions, although no significance is claimed for this fact.

The authors point out that measurements of air pollution during periods of 24 or 48 hours do not necessarily indicate the hazard to which the population may be exposed, since considerable variations may occur during that period. *A. Garland*

238. **Cancer of the Uterine Cervix and Social Conditions**
P. STOCKS. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 487–494, Dec., 1955. 7 refs.

A special medical inquiry instituted in 1950 by the Registrar-General for England and Wales regarding the site of origin of cancers described on death certificates as " uterine ", without designation of the particular part of the uterus affected, has provided more accurate statistics on the incidence of cancer of the cervix. The death rates for this disease for 1950 and 1951 now available show that infertile married women suffered about double the mortality of single women at corresponding ages, while the comparative mortality ratio for fertile married women (103) was only 23% above that for infertile married women (84). Mortality from this cause in the Registrar-General's Social Class V was 30% greater than in Social Classes III and IV and 70% greater than in Classes I and II. It is stated that the lower fertility of Classes I and II (professional and administrative) accounts for only a small proportion of these differences.

Data on the first 155 cases of cancer of the cervix at ages 45 to 74 and on 718 hospital patients without cancer, collected during a current survey in the Liverpool area for the British Empire Cancer Campaign, show that among the patients with cancer there was a pronounced excess of women married before the age of 20. The number of confinements among those with cancer shows no excess over expectation for those married before 25 years, but a considerable excess among those married

later, these findings largely agreeing with those of other workers. It is concluded that sexual intercourse starting at an early age and continued over many years may be an important factor in the causation of cancer of the cervix, although from other studies, notably among Jewish women in Israel, it appears that this need not be the case if marital hygiene is meticulously observed.

The author has also examined the effect of other environmental conditions by comparing the comparative mortality ratio (C.M.R.) for 48 English county boroughs with the various social indices. This showed that towns with a high C.M.R. tended to have a greater number of persons per room and a larger proportion of men in Social Classes IV and V; they are also characteristically seaports or textile-manufacturing towns. It is suggested that the latter observation may be related to the occurrence of a high rate of cancer of the skin among mule-spinners, fishermen, and workers exposed to tar or pitch.

Richard Doll

239. **Vaccinia versus Poliomyelitis?**
D. P. MACIVER. *Lancet* [*Lancet*] **1**, 226–228, Feb. 4, 1956.

In three districts in Surrey with a total estimated population of 87,340 the number of children born between the years 1946 and 1954 totalled 11,842, and of these, 53% were vaccinated against smallpox. While the greatest variation in the annual vaccination rate for one district was 30 to 64%, the over-all rate for the three districts remained fairly constant. The present author has attempted to determine whether there is any relationship between vaccination and paralytic poliomyelitis. He points out that if there is no association then no significant difference would be expected between the number of cases of poliomyelitis occurring in vaccinated and in unvaccinated children. He found that since 1946 there had been 21 cases of paralytic poliomyelitis in unvaccinated children under the age of 5 years but only 4 among vaccinated children. This contrast became more marked when the figures for children under 3½ years of age were compared. In that age group there were 17 cases of paralytic poliomyelitis in the unvaccinated children, and 2 in the vaccinated. Of the 2 vaccinated children in whom poliomyelitis developed, one died from the disease 4 days after vaccination; the other had received a third injection of diphtheria–pertussis prophylactic 14 days previously and this may have provoked the disease.

J. E. M. Whitehead

240. **Serological Epidemiology of Poliomyelitis. Distribution of Immunity to Poliomyelitis Virus**
R. J. FALLON. *Lancet* [*Lancet*] **1**, 65–69, Jan. 14, 1956. 11 figs., 18 refs.

Previous observations having shown that in some 18 districts in England and Wales no case of poliomyelitis had been notified for 30 years (1922–52), it has been suggested that this was owing to the absence of poliomyelitis virus in these communities. In the present investigation, reported from the University of Liverpool, samples of serum were collected from 78 children aged 0 to 14 years in Bettws-y-Coed, a Welsh village of 750 persons, from which no cases of poliomyelitis have ever been notified (that is, since the disease became notifiable in 1912). For comparison, samples of serum were collected from 71 children of the same age groups in Liverpool (population 786,000) where poliomyelitis has occurred with increased frequency in the last few years (135 cases in 1951). The sera from the two communities were examined for the presence of neutralizing antibodies against poliomyelitis virus Types 1, 2, and 3, using either monkey kidney or HeLa cell tissue cultures.

Only 8 of the 78 children from Bettws-y-Coed were without antibodies at a serum dilution of 1 in 10, and of these 5 were under 2 years of age. Antibodies to all three types of virus were present in 26 of the children, although antibodies to Type-3 virus occurred least frequently. The findings in respect of the Liverpool children were essentially similar, although antibodies appeared to be developed at a slightly later age than in Bettws-y-Coed. The significance of this serological evidence of widespread and early infection in two communities with strikingly different rates of clinical poliomyelitis is discussed, and the author's findings compared with those reported for two widely separated cities, namely, Winston-Salem (U.S.A.) and Cairo (Egypt).

[The number of samples of serum from each age group was necessarily small and must thus limit the significance of the figures of the prevalence of antibodies at each year of age.]

J. E. M. Whitehead

241. **Effect of Booster Inoculations on the Serologic Status of Children Vaccinated with Poliomyelitis Vaccine**
G. C. BROWN. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **45**, 1401–1408, Nov., 1955. 6 figs., 5 refs.

The effect was studied of a booster dose of poliomyelitis vaccine on 119 children in three counties of Michigan who had received the recommended primary inoculations with the Salk vaccine a year before. The serum antibody titres against the 3 types of virus were determined by neutralization tests in tissue cultures after the booster dose and compared with those observed before and after primary vaccination. There was a definite increase in the serum antibody titres after the booster inoculation, although titres of 1 in 1,024 were observed in fewer children than was the case after primary vaccination. Because of a difference in the antigenic potency of the original vaccine a good response to the primary inoculation was obtained in the children of only one county; the booster dose, however, was found to be especially effective in the two counties in which the primary response had been poor. After the booster dose of vaccine the serum antibody titres were about the same in all groups.

A more sensitive technique of determining antibody titre was used in an additional group of 18 younger children. In this group a very satisfactory antibody titre in response to the primary vaccination was followed by a gradual decline over the intervening year to a level only slightly higher than that before vaccination. The booster inoculation had a much more pronounced effect on the serum antibody titres in this group of children than in the other groups.

A. Ackroyd

Industrial Medicine

242. **Studies on the Toxicology of N-Nitrosodimethylamine Vapor**
K. H. JACOBSON, H. J. WHEELWRIGHT, J. H. CLEM, and R. N. SHANNON. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **12**, 617–622, Dec., 1955. 1 fig., 12 refs.

The vapour of N-nitrosodimethylamine was found at the U.S. Army Chemical Corps Medical Laboratories to be highly toxic to animals. The LC_{50} for rats exposed to the vapour for 4 hours and observed for 14 days was estimated to be 78 parts per million (p.p.m.) in air, and for mice to be 57 p.p.m. Of 3 dogs exposed to a vapour concentration of 16 p.p.m. for 4 hours, only one survived. The immediate effect was irritation of the gastro-intestinal tract with nausea, vomiting, and diarrhoea. Leucopenia developed swiftly, accompanied by a disruption of the mechanism of blood coagulation, with bleeding into the wall of the stomach and intestines, into the peritoneal cavity, and elsewhere. The body temperature rose. The liver showed signs of damage within a few hours of exposure, marked central necrosis of the lobules and also haemorrhages into the liver substance being found at necropsy. Death occurred within the first 4 days after exposure. The dog which survived exposure to a vapour concentration of 16 p.p.m. apparently recovered completely, but when killed 7 months later it was found to have residual liver damage.

The literature of industrial intoxication with this substance is reviewed, and it is recommended that exposure of workers to the vapour should be prevented. The suggestion is made that water or an aqueous acid solution may effectively remove any liquid spill. The odour of the vapour closely resembles that of the methylated derivatives of hydrazine. *M. A. Dobbin Crawford*

243. **Toxicity of Naphthenic Acids and their Metal Salts**
W. T. ROCKHOLD. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **12**, 477–482, Nov., 1955. 9 refs.

At the Occupational Health Field Headquarters (U.S. Public Health Service), Cincinnati, the author has investigated the toxicity of the naphthenic acids; these occur as a by-product in the refining of petroleum and are monobasic carboxylic acids with acid numbers ranging from 200 to 300. The metallic salts are widely used in industry: the lead, cobalt, manganese, and zinc naphthenates as paint driers; the copper and zinc naphthenates as fungicides; the sodium, potassium, and ammonium naphthenates as emulsifiers and demulsifiers; and the lead and aluminium naphthenates as lubricants.

The toxicity of two naphthenic acid fractions and of seven heavy metal naphthenates was tested on rats by oral and by peritoneal administration. Given by the mouth, the calcium, copper, manganese, and zinc naphthenates were found to be practically non-toxic, the LD_{50} being greater than 6 mg. per kg. body weight, as was also lead naphthenate (LD_{50} 5·1 g. per kg.). Cobalt naphthenate (LD_{50} 3·9 g. per kg.) was moderately toxic, while phenyl mercury naphthenate, containing 10% mercury, was slightly toxic (LD_{50} 0·39 g. per kg.). The substances produced gastro-intestinal disturbances, and death occurred on the third or fourth day. The toxicity of the naphthenic acid fractions and the lead and phenyl mercury naphthenates when given by the intraperitoneal route was 10 times greater than when they were given by mouth. Following oral administration, 40% of the lead was excreted within 3 days, mainly in the faeces, the ratio of urinary to faecal excretion being approximately 1 to 100. Very small doses of lead naphthenate—based on the percentage of lead permitted in commercial paints—produced a threefold increase in the lead deposit in the hair, but there was no significant reduction in the cystine content of the hair and no lead was found stored in the liver. The author comments that the naphthenic acids and some of their metallic compounds, notably copper naphthenate, have been reported to be skin irritants, but the cutaneous effect was not studied in this investigation.

M. A. Dobbin Crawford

244. **Studies in Vanadium Toxicology. III. Fingernail Cystine as an Early Indicator of Metabolic Changes in Vanadium Workers**
J. T. MOUNTAIN, F. R. STOCKELL, and H. E. STOKINGER. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **12**, 494–502, Nov., 1955. 8 refs.

As a result of the observation that the ingestion of vanadium by rats resulted in a decrease in the cystine content of their hair, the authors have investigated, at the Occupational Health Field Headquarters, Cincinnati, the cystine content of fingernail clippings from three groups of people: (1) workers exposed to vanadium in different forms, (2) a wide variety of subjects having no known industrial exposure to vanadium, and (3) a group of hospital patients with different types of organic disease. Some 850 specimens of fingernails were analysed. The normal average content of cystine in the fingernails is 10% and this value is very constant, a decrease of 1% being judged abnormal. In the workers exposed to vanadium it was found that as the urinary excretion of vanadium increased, so the cystine content of the fingernails diminished. Of one group of 20 vanadium workers with an average excretion of 30 μg. of vanadium per litre, the cystine content of the fingernails was less than 9% in 15.

As the nails take some 3 to 3½ months (1 mm. per week) to grow from base to tip, this test is not applicable in conditions of acute exposure; its chief value is claimed to be in the identification, in cases of chronic exposure, of

vanadium absorption of a degree less than will produce clinical signs of intoxication. It is assumed that the decrease in the cystine content of the fingernails is the result of an alteration in the metabolic processes of the liver, a similar decrease being found in patients with chronic cirrhosis of the liver, certain types of cancer, and arthritis of long standing. The authors suggest that determination of the cystine content of the fingernails may be used as a screening test of disturbed body metabolism. The technique employed is described in detail and the results for the various groups are tabulated.

M. A. Dobbin Crawford

245. **Occupational Deafness. Medical, Medicolegal, and Compensation Aspects and Constructive Approach to Problems**

A. I. GOLDNER. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **12**, 643–656, Dec., 1955. 10 figs., 21 refs.

The great bulk of occupational deafness is subclinical and is recognized only when audiometric examination or superimposed infection or accident draws attention to it. An analysis of the findings in 403 shipyard workers shows that in the average case of occupational deafness, whereas simple conversational voice may still be heard at 20 feet (6·1 metres), hearing is usually defective by the whisper test; there is a diminution of both air and bone conduction, the normal proportions being preserved (" diminished positive response " to Rinne's test); there is a reduction of absolute bone conduction (diminished Swabach reaction); and the tuning fork is not generally lateralized (Weber's test). The audiometric curve is typical and should be fairly symmetrical except in the rare instances of unequal exposure of the ears or in cases of superimposed pathology. This type of deafness also occurs as a result of degenerative disease commonly found in the elderly, of syphilis and other infectious diseases, of drug intoxication—for example, streptomycin—and of Ménière's disease, head injuries, and neoplasms.

The differential diagnosis, particularly from presbyacusia, may be most difficult in evaluating compensation, the part played by presbyacusia being easily overestimated. The auditory pattern in cases of established mixed conductive and occupational deafness is quite different. Marked deafness and inability to hear conversation are the rule rather than the exception. The lower frequencies are depressed in intensity and frequently inaudible, and bone conduction is generally better than air conduction. A noisy environment is quite well tolerated and without undue fatigue.

Where occupational deafness is a hazard, pre-employment examination should include audiometric evaluation. A bilateral hearing impairment of up to 40% and even total loss of hearing in one ear may exist without the patient's knowledge and be demonstrable only by a careful test of the hearing with audiometric evaluation. Otitis media and damaged eardrums should be a bar to employment on noisy work, but established occupational deafness is not necessarily so, since it may be that the maximum damage has been done, though a pre-employment audiogram is a necessity. Workers with otosclerosis often seem to tolerate noise better than others, and to suffer less fatigue, but they may incur additional injury from a noisy environment. The elderly should be employed with caution.

It is stressed that frequent audiometric tests of new workers in their first years of employment would do much to eliminate those who are susceptible to noise before permanent damage has been done. Possible preventive measures include the regulation of hours of exposure to noise, the avoidance of confined spaces, the use of ear protectors, and the elimination of vibration from machinery.

M. A. Dobbin Crawford

246. **Pneumoconiosis in Coal-miners. Aseptic Cavitation in Massive Fibrosis. Simple Forms of Pneumoconiosis without Radiological Signs.** (La pneumoconiose des mineurs de charbon. L'excavation aseptique des fibroses massives. Les formes simples radiologiquement muettes)

C. GERNEZ-RIEUX, E. BALGAIRIES, A. COLLET, and P. FOURNIER. *Presse médicale* [*Presse méd.*] **63**, 1551–1554, Nov. 16, 1955. 8 figs., 2 refs.

The authors report 18 cases of massive fibrosis in coal-miners with cavitation, one fatal case being described in great detail. The clinical findings were similar to those recorded by other authors, namely, recurrent episodes of " melanoptysis ", usually associated with a febrile attack. Analysis of the fluid obtained by transpleural puncture of the cavities showed that it had a protein content similar in quantity to that of serum and with a similar distribution of the various fractions, and that it was relatively rich in lipids and cholesterol. Its black colour was due to a carbon content which rose as high as 50%. The silica content was extremely low. In only one case were there tubercle bacilli in the sputum and in this case fluid aspirated from the cavity also contained tubercle bacilli, whereas that from a mass in the contralateral lung was sterile. On pathological examination the authors found very little obliterative endarteritis. There were necrotic lesions of the bronchioles, explaining the communication between the inside of the mass and the bronchial tree, but the origin of the liquefaction in these cases remains obscure; since the fluid is sterile the liquefaction is not due to bacterial action, and since there is little endarteritis it is not likely to be ischaemic in origin. The rapid filling up of the cavities after evacuation is also difficult to reconcile with ischaemia.

The authors also report 6 cases in which localized nodular shadows were present in the lung radiographs of men with a history of dust exposure. Lobectomy was carried out on the assumption that the lesions were tuberculous, but on histological examination of removed tissue there were mixed dust nodules without evidence of tuberculosis.

Lastly the authors report 3 cases in which scanty coal foci were found at necropsy although there had been no radiological evidence of pneumoconiosis, showing that early coal pneumoconiosis cannot always be detected radiologically.

C. M. Fletcher

Anaesthetics

247. **A Physiological and Clinical Study of a Steroid with Anaesthetic Properties: 21-Hydroxypregnandione Sodium Succinate.** (Étude physiologique et clinique d'un stéroïde anesthésique: le succinate sodique de 21-hydroxyprégnandione)
H. Laborit, P. Huguenard, C. Douzon, B. Weber, and R. Guittard. *Presse médicale* [*Presse méd.*] **63**, 1725–1727, Dec. 14, 1955. 12 figs., 8 refs.

The authors describe animal and human experiments carried out at the Hôpital Vaugirard, Paris, to determine the anaesthetic properties of 21-hydroxypregnandione sodium succinate ("viadril"). Using dogs, rats, and mice they demonstrated that the steroid was free from gross effects upon the sympathetic and parasympathetic nervous systems when given slowly. It caused tachycardia and bradypnoea, but no hypotension or changes in the electrocardiogram, nor was there any notable difference in the usual response to the subsequent administration of adrenaline, noradrenaline, or acetylcholine, or to pressure upon the carotid sinus. It did, however, cause copious salivation in dogs.

As an anaesthetic agent it was feeble compared with the barbiturates, a dose of 50 mg. per kg. body weight producing sleep of only 15 to 30 minutes' duration in dogs and rats, while double that dose failed to prevent shivering during the subsequent induction of hypothermia. The most remarkable effect of the steroid was in potentiating the action of other narcotic drugs; whereas in rats a dose of 150 mg. of thiopentone per kg. body weight normally produced only 10 minutes' sleep, the addition of 25 mg. of the steroid per kg. body weight invariably caused fatal respiratory depression. Although having very little hypothermic effect itself, it strongly augmented the effect of the "lytic cocktail" in producing hypothermia and abolishing shivering.

Because of the similarity of the structural formula of the steroid to that of deoxycortone acetate it was considered necessary to investigate its effect upon electrolyte balance before attempting to use it in clinical practice. This was done in 3 patients with delirium tremens (whose metabolism was not complicated by the concurrent administration of conventional anaesthetic drugs) who were controlled for periods of up to 24 hours with total doses of 8 to 10 g. of the steroid, when barely detectable changes were observed in the electrolyte levels; the drug was given by subcutaneous perfusion together with hyaluronidase. As in the animal experiments it was found to be a feeble narcotic but had a pronounced effect in potentiating the effects of other anaesthetic agents and hypothermic drugs. The authors also claim to have produced longer, deeper, and more stable anaesthesia by giving natural hormones (such as insulin and androgens) together with the new steroid. They conclude by suggesting that perhaps the greatest value of the drug will prove to be in elucidating the changes in hormonal balance which occur in naturally hibernating animals, a better understanding of which may make possible the production of true "hibernation" in man. Meanwhile, although the drug is undoubtedly a weak anaesthetic it is, in the authors' words, "the first time that we have had in our possession a steroid, that is to say a substance of strictly biological structure, which is capable of producing anaesthesia without seriously disturbing peripheral cellular equilibrium".

Donald V. Bateman

248. **Respiratory Hazards of Opiates and Other Narcotic Analgesics**
J. E. Eckenhoff, M. Helrich, M. J. D. Hege, and R. E. Jones. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 701–708, Dec., 1955. 5 refs.

This paper from the Hospital of the University of Pennsylvania describes experimental observations on the prolonged effect of certain commonly employed narcotics on respiratory rate, minute and tidal volume, "alveolar" carbon dioxide pressure (pCO_2), and the response to endogenously accumulated carbon dioxide in human subjects. The drugs tested were morphine, pethidine, codeine, "nisentil" (1 : 3-dimethyl-4-phenyl-4-propoxypiperidine), "dilaudid" (dihydromorphinone), methadone, and "seconal" (quinalbarbitone), given in therapeutic dosage injected intramuscularly. Observations were made before administration and repeated 30 minutes and one hour after administration and hourly thereafter.

Elevation of pCO_2 invariably accompanied opiate administration in the 21 subjects studied. Respiratory minute volume was diminished in 19 of the 21, and respiratory tidal volume was diminished in 15. Respiratory rate was found to be an unreliable guide to respiratory depression. The respiratory response to endogenous carbon dioxide was depressed by opiates in all but one subject, the depression continuing after all other respiratory measurements had returned to normal.

In 3 subjects receiving barbiturates pCO_2 was unchanged, respiratory rate, tidal, and minute volumes were not significantly depressed, and the response to carbon dioxide was not depressed at all.

It is stressed that when the respiratory centre is already depressed, as in pulmonary emphysema, cerebral arteriosclerosis, cerebrovascular accident, senility, congestive heart failure, and in anaesthesia, the unwise use of opiates may precipitate acute respiratory depression. The prime indication for the use of opiates should be pain; they should not be used for inducing sleep or reducing emotional stress, for which barbiturates are just as good and less hazardous.

B. L. Finer

249. **Hyaluronidase in Epidural Analgesia**
D. B. Scott. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **28**, 187–193, April, 1956. 2 figs., 8 refs.

250. **A Comparative Clinical and Statistical Study of Thiopental and Thiamylal in Human Anesthesia**
R. M. TOVELL, C. C. ANDERSON, M. S. SADOVE, J. F. ARTUSIO, E. M. PAPPER, C. S. COAKLEY, F. HUDON, S. M. SMITH, and G. J. THOMAS. *Anesthesiology* [*Anesthesiology*] **16**, 910–926, Nov., 1955. 46 refs.

A comparative investigation is reported of the effects of thiopentone and of thialbarbitone (" surital ") as used in hospital practice for anaesthesia. Altogether 9 departments of anaesthesia in the United States and Canada participated in the investigation and each drug was given to more than 1,000 patients. The investigation was carefully controlled and the results were analysed for statistical significance. A large number of factors, including the potency and duration of action of the drugs and the incidence of nystagmus, apnoea, arrhythmia, hiccup, trismus, retching, and vomiting were evaluated. The results showed clearly that for anaesthesia in human beings the two drugs were interchangeable. Laryngospasm occurred in almost the same number of cases with either drug, but it lasted significantly longer after administration of thialbarbitone than after thiopentone. The incidence of dizziness after operation was also higher with thialbarbitone anaesthesia.

[A trial such as this is worth hundreds of " clinical impressions ".] *Ronald Woolmer*

251. **Ethyl Chloride as a Gaseous Anaesthetic**
W. H. J. COLE. *Anaesthesia* [*Anaesthesia*] **11**, 156–159, April, 1956. 1 ref.

252. **Acid Base Balance and Anaesthesia**
B. G. B. LUCAS and E. H. MILNE. *Thorax* [*Thorax*] **10**, 354–358, Dec., 1955. 6 figs., 12 refs.

The acidosis which occurs during anaesthesia was formerly thought to be metabolic in origin and due to inefficient carbohydrate breakdown in the unconscious state. It has recently been suggested, however, that it is due to defective ventilation, and in order to confirm or refute this concept the authors have studied the acid–base changes in 166 anaesthetized patients undergoing operation at University College Hospital, London. The degree of acidosis was estimated from the tension of carbon dioxide in the blood, calculated from the total carbon dioxide content and *p*H of the blood. As the authors point out, before the advent of modern methods of anaesthesia respiration was the main guide to depth of anaesthesia, so respiratory depressants were avoided for obvious reasons. Now, however, with the use of barbiturates, pethidine, and muscle relaxants respiratory depression is unavoidable.

The normal minute volume of the unanaesthetized subject at rest is about 6 litres. In some of the patients in this study who were breathing spontaneously the minute volume was as low as 1½ litres, but in spite of this there was no change in blood oxygenation, probably because they were breathing a 50% oxygen–nitrogen mixture. The elimination of carbon dioxide, however, was grossly inadequate and severe acidosis often occurred (*p*H 6·9). Positive pressure controlled artificial respiration could maintain a normal acid–base balance, but for this a minute volume of 14 litres was required; this type of respiration is thus relatively inefficient because it is unphysiological. The pressure necessary for ventilation is greatly increased in the Trendelenburg position. The lateral position, especially with the table " broken ", also increased the acidosis. The development of acidosis was accompanied at first by a rise in blood pressure, but this soon fell, with signs of shock.

The authors sum up as follows. The unconscious patient, during modern anaesthesia, is incapable of ventilating himself efficiently. The minute volume required to prevent acidosis during artificial respiration is greater than that of normal respiration and greater still in the lateral or Trendelenberg positions and in intrathoracic surgery. In these cases, if vigorous overventilation is not possible throughout, operative pauses should be made from time to time to allow of maximum ventilation. The harmful effects of respiratory acidosis are briefly discussed. *W. Stanley Sykes*

253. **An Investigation of Problems of Acid–Base Equilibrium in Hypothermia**
E. G. BREWIN, R. P. GOULD, F. S. NASHAT, and E. NEIL. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 177–214, 1955. 24 figs., 45 refs.

The investigation here reported from Guy's and the Middlesex Hospitals, London, was concerned with the physiology of hypothermia and rewarming as related to the problems confronting the cardiac surgeon who uses hypothermia in conjunction with temporary circulatory arrest. It consisted of four parts: (1) a study of the physico-chemical changes occurring in blood equilibrated *in vitro* with carbon dioxide at various tensions and at temperatures from 37° to 26° C.; (2) a study of the changes in acid–base equilibrium occurring in dogs cooled to 26° C. and then rewarmed to 37° C., without surgical interference; (3) a study of the physico-chemical changes occurring in dogs and human patients subjected to cooling, thoracotomy, and circulatory arrest, followed by re-establishment of the circulation and rewarming to 37° C.; and (4) a consideration of the therapeutics and prophylaxis of disturbances of acid–base balance in operative hypothermia.

It was found that although the solubility of CO_2 in blood *in vitro* is greater at 26° C. than at 37° C. the *p*H remains unchanged for any given tension of CO_2. This is due to the fact that ionization of the blood proteins is diminished at the lower temperature, so that more base is available for bicarbonate formation and the ratio of bicarbonate to carbonic acid is unaltered. In experiments *in vivo* on the other hand it was shown that with spontaneous breathing lactacidosis occurred during cooling from 37° to 26° C., this change being only partly reversed on warming. In animals ventilated artificially throughout this residual metabolic acidosis was rather more severe, while both in dogs and in man the development of metabolic acidosis was exacerbated when arrest and restoration of the circulation were carried out before rewarming.

The cause of the lactacidosis is obscure, but since it may be as severe as the acidosis of diabetic coma its

treatment and prevention are of considerable practical importance. Administration of bicarbonate solutions may be temporarily effective, but the basic cause must be determined before preventive measures can be taken. It is probable that as a result of circulatory arrest and anoxia the function of the liver is profoundly depressed. When the inferior vena cava was clamped in dogs under hypothermia the central hepatic venous pressure rose markedly. With continuous aspiration of blood from the vena cava and its return to the circulation via the femoral artery the hepatic venous pressure was reduced and residual metabolic acidosis on rewarming was negligible. Moreover, structural changes which were present in the liver in animals not so treated were not seen when hepatic congestion was prevented, and liver function, as measured by the galactose tolerance test, was almost normal, a severe disturbance being found in association with metabolic acidosis. Further investigation of human liver function during cardiac surgery under hypothermia is clearly indicated. *B. L. Finer*

254. **Adrenal Cortical Function in Hypothermia**
R. H. EGDAHL, D. H. NELSON, and D. M. HUME. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 715–720, Dec., 1955. 3 figs., 6 refs.

This paper from the U.S. Naval Medical Research Institute, Bethesda, Maryland, describes investigations into the adrenal cortical reaction pattern during hypothermia and rewarming in mongrel dogs anaesthetized with sodium pentobarbitone or thiopentone and ether. Blood was obtained from the right adrenal vein by means of a cannula and repeated estimations of the 17-hydroxycorticosteroid content made. Hypothermia was produced by (1) exposure to an external temperature of −10° C.; (2) cooling the blood in an external arteriovenous shunt with ice water at 4° C.; or (3) total immersion in ice water at 4° C. Rewarming was accomplished by immersion in water at 45° C. At all temperatures below 30° C. positive pressure respiration was instituted.

During hypothermia produced by any method in 11 dogs 17-hydroxycorticosteroid secretion was reduced; it recovered on rewarming, rising above the control level in about half the dogs. Constant infusion of ACTH (corticotrophin) during hypothermia in 10 dogs made no difference to this fall in secretion, nor did maintenance of the blood pressure at a constant level in 2 dogs by infusion of noradrenaline. The blood ACTH level was estimated during hypothermia in 2 dogs and was found to be reduced. In further experiments cold was applied locally to one adrenal gland in 2 dogs, a normal body temperature being otherwise maintained. A significant fall in corticoid production was noted, with a rapid return to normal on rewarming.

The authors state that it appears likely that in hypothermia there is a depression of ACTH secretion and adrenal corticoid output and also of tissue uptake, so that there is no relative deficiency of the hormones in the tissues. The immediate return of secretion to normal on rewarming indicates that the adrenal gland is not damaged by hypothermia. *B. L. Finer*

255. **Hypothermia for Neurological Operations**
M. M. BURROWS, J. W. DUNDEE, I. L. FRANCIS, S. LIPTON, and C. B. SEDZIMIR. *Anaesthesia* [*Anaesthesia*] **11**, 4–18, Jan., 1956. 8 figs., 11 refs.

In this paper from the Walton Hospital, Liverpool, and the University of Liverpool experience with hypothermia in 50 neurosurgical cases is reported. Premedication was with 50 mg. of chlorpromazine, which was combined with 50 mg. of pethidine where consciousness was normal; induction was with 200 to 400 mg. of thiopentone. After administration of succinylcholine and anaesthetization of the larynx oral intubation with an armoured latex tube was carried out. Anaesthesia was maintained with gas and oxygen at 10 litres a minute total flow through an Ayre's T-piece, supplemented with doses of thiopentone and chlorpromazine if necessary; indications for chlorpromazine included peripheral vasoconstriction, slow cooling, and shivering. Altogether 12 rubber ice-bags were applied over the whole body, particularly over large arteries, and a jaconet pillow-case containing ice was placed under the patient. Blood pressure, pulse, and rectal temperature were recorded at 10-minute intervals. When hypotension was insufficient, despite cooling and positioning, for operations on vascular lesions an infusion of 0·1% solution of "arfonad" (trimetaphan) was given to reduce pressure to 70 to 80 mm. Hg. Optimum temperature was thought to be 30° C., and the average time taken to reach this was 92 minutes. Ice-bags were removed to allow for an "after-drop" of about 2° C., this being greater in children and obese patients. Rewarming was gradual; blankets were not used and shivering was treated by injection of 2 mg. of levorphan with or without chlorpromazine, temperatures of 36° to 38° C. being reached in 6 to 8 hours. The authors emphasize the need for a rapid method of rewarming children. Trimetaphan was required by 23 patients, most of them in younger age groups undergoing operation for vascular anomalies. In 2 cases there was resistance to the drug, and in one apnoea occurred after 2 g. of trimetaphan had been given over 40 minutes.

Complications included extrasystoles, mostly in older patients, heart block in one case at a temperature of 26° C., and a fall in blood pressure in 2 cases; respiratory depression occurred in 3 cases, and reactionary haemorrhage in one case. There were 5 deaths, 2 from pulmonary embolism, 2 from aspiration pneumonia when hypothermia was continued into the postoperative period, and one death from heart block. No skin complications attributable to the contact of ice-bags were observed.

The authors consider that the advantages of the method include a contracted brain, low intraventricular pressure, no troublesome haemorrhage, and greater freedom for the surgeon. *Raymond Vale*

256. **Intercostal Nerve Block in Upper Abdominal and Chest Surgery**
H. A. BENNETT, H. C. DODSON, and B. J. BAMFORTH. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **35**, 123–130, March–April, 1956. 7 refs.

Radiology

257. **Combination of *X* Rays and "Sanamycin" [Actinomycin C] in the Treatment of Diseases of the Haematopoietic System.** (Kombination von Röntgenstrahlen und Sanamycin bei der Behandlung von Erkrankungen des blutbildenden Systems)
D. MAGNUS and K. ZEITLER. *Strahlentherapie* [*Strahlentherapie*] **98**, 413–419, 1955. 15 refs.

The authors report on their 18 months' experience of the use of "sanamycin" (actinomycin C) at the University Surgical Clinic, Munich, in the treatment of 13 cases of Hodgkin's disease, 2 of lymphatic leukaemia, and one of myeloid leukaemia. Courses totalling 5,000 to 8,000 μg. were given, in doses of 200 μg. per day intravenously on 5 days per week, in combination with conventional *x*-ray therapy. It is claimed that the substance is free from the damaging effects on the bone marrow attributed to urethane, T.E.M., and busulphan ("myleran"). In larger doses (1,000 μg. or more), however, it is said to cause loss of hair, neuritis, and pigmentation, but in the dosage used in this study there were practically no undesirable complications.

In general, the patients showed improved appetite, gain in weight, and absence of *x*-ray sickness, while pyrexia and sweating were well controlled. It was doubtful whether the use of sanamycin allowed a lower dosage of *x* rays, and the impression was gained that the enlarged nodes did not resolve any faster; on the other hand it was thought to exert a beneficial effect on the pain, dyspnoea, and pyrexia. In the one case of myeloid leukaemia it brought about a lowering of the leucocyte count but did not affect the size of the spleen. As the authors point out, too short a time has elapsed to allow of any useful evaluation of the possible effects of the drug on the period of survival.

J. Walter

RADIODIAGNOSIS

258. **The Value of the Recumbent Oesophagram in Assessing Left Auricular Enlargement**
J. KAYE, B. VAN LINGEN, M. J. MEYER, and M. ZINOBER. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 693–697, Dec., 1955. 7 figs., 5 refs.

It has been claimed that "the recumbent oesophagram is a more sensitive method for the determination of left auricular enlargement than a similar study in the erect position". In order to test this claim the authors, working at Johannesburg General Hospital, South Africa, have measured the backward displacement of the barium-filled oesophagus in the right anterior oblique position in 50 cases of non-cardiac disease and 50 with mitral disease, radiographs being taken in both the recumbent and erect positions. For the latter the tube–film distance was 64 inches (1·6 metre), whereas for the recumbent position it was about 28 inches (70 cm.); but even allowing for this difference in tube–film distance, the authors showed that there was greater backwards displacement in the recumbent position than in the erect position, and that this was true for both groups of patients. The method of measurement is described and illustrated diagrammatically.

In the former group the mean posterior displacement of the oesophagus in the recumbent position was 14·4 mm. and in the erect position 7·9 mm. Similar results were obtained in the patients with mitral disease, the mean degrees of displacement in this group being 26·6 and 19·6 mm. respectively. The authors point out, however, that these are merely average figures and that some of the patients suffering from valvular disease showed the same or less displacement than some in the other group. They conclude, therefore, that the recumbent oesophagram affords no greater accuracy in diagnosis of mitral-valvular disease than that taken in the erect position, and point out that in fact their figures show that the differential diagnosis between the normal heart and one with a mitral lesion is more accurate when based on films taken in the erect than in the recumbent position. Secondly, they show that the degree of displacement in the erect or recumbent views is not as accurate in the diagnosis of left auricular enlargement as the presence of two or more of the following signs: a left auricular appendage visible in the postero-anterior view, a double density visible in the postero-anterior film, and evidence of left auricular enlargement in the left and right anterior oblique views. *L. G. Blair*

259. **The Uptake of Radioactive Phosphorus in Normal Breast and Breast Tumors.** [In English]
N. N. DAS GUPTA, K. L. BHATTACHARYA, R. DUTT CHOUDHURI, A. BOSE, and P. K. DE. *Acta radiologica* [*Acta radiol. (Stockh.)*] **45**, 69–80, Jan., 1956. 4 figs., 11 refs.

From the Chittaranjan Hospital, Calcutta, the authors report their experience with radioactive phosphorus (^{32}P) in the treatment of 48 patients with palpable breast tumours. Each patient received an intravenous dose of 0·01 μc. of ^{32}P (as Na_2HPO_4) per g. body weight and the radioactivity directly over the tumour and at the corresponding position on the opposite breast subsequently determined at intervals for 48 hours by means of a thin-walled Geiger-Müller counter. The counting rate over the tumour was expressed as a percentage of the counting rate over normal breast tissue 2 hours after administration of ^{32}P. The mean of these percentage counting rates over the 48 hours was also calculated.

In a few patients who were subjected to mastectomy the concentration of ^{32}P in the tumour and in tumour-free breast tissue 48 hours after its administration was determined directly by ashing weighed specimens in a

muffle furnace at 600° C., dissolving the resulting ash in 2N hydrochloric acid, and measuring the radioactivity of the solution, counts per minute being converted into absolute activity in microcuries by comparison with a simulated standard ^{32}P source (^{238}uranium in equilibrium with ^{234}thorium and ^{234}protoactinium).

Maximum counting rates over normal breast tissue, benign tumours, and malignant tumours were obtained about 20 minutes after injection. The fall-off in surface counting rate was at first rapid (effective half-life 2 hours), then becoming slower (effective half-life 72 hours) with both simple and malignant lesions. Of the 48 cases studied, in 20 the tumour was histologically malignant and in 17 of these the mean count over the tumour was more than 130% of that over the normal breast. In one case of malignant tumour the count was less than 110%, while in 3 cases of ulcerated and infected tumours the count was higher than 300%. Of the 28 cases of benign tumour, in 23 (82%) the count was less than 130%. High counting rates were also found in other diseases of the breast (cystic hyperplasia and tuberculosis).

[As an aid to the diagnosis of malignancy in tumours of the breast ^{32}P has little to offer. However, it will probably prove to be a useful tool in the diagnosis of malignant melanoma of the eye.] *Norman Mackay*

260. **Thoracic Aortography by Percutaneous Transcarotid Catheterization**
D. SUTTON. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **7**, 172–183, Jan., 1956. 15 figs., 12 refs.

In view of the widening scope of thoracic vascular surgery a satisfactory method for the radiological visualization of the thoracic aorta and great vessels is increasingly required. The author here describes the technique devised at St. Mary's Hospital, London, to achieve this by percutaneous catheterization of the carotid artery; the method is based on that described by Seldinger (*Acta radiol. (Stockh.)*, 1953, **39**, 368) and employs the same instruments. The procedure has so far been attempted 13 times in 12 cases, and was successful in all 12 at the first attempt, although a second and post-operative attempt in one patient failed.

Either of the carotid arteries may be used; in either case the catheter enters the aortic arch and almost invariably descends into the ascending aorta. The precise siting of the catheter tip is important: it must be placed midway down the ascending aorta, and its position should be checked by a control film taken after the injection of 5 ml. of 50% diodone. For the actual examination 30 to 40 ml. of 70% diodone is used, the time of injection being 2 to 3 seconds. The examination was usually carried out under general anaesthesia, except in one case in which pethidine was used. As a rapid cassette changer was not available, films were taken in one plane only at the rate of approximately four in 6 seconds.

As regards complications, it is recommended that formation of a haematoma should be guarded against by manual compression after the catheter has been inserted, such pressure being kept up for some 5 minutes after its withdrawal. Finally a firm pressure bandage is applied and instructions given that this must be watched for some hours after the patient returns to the ward. In one case, on the day after the investigation, the patient complained of some disturbance of vision; this was thought to be due to a small thrombus in the distribution of the posterior cerebral artery. There has been one death, but this was attributed to the anaesthetic and in no way connected with the aortography. Of the 12 patients investigated, 6 were cases of coarctation of the aorta and 6 of aneurysm or suspected aneurysm; but the author lists the possible indications for the procedure as follows: (1) coarctation of the aorta; (2) patent ductus arteriosus; (3) thoracic aortic aneurysm; (4) congenital anomalies of the great vessels; and (5) acquired lesions of the innominate, left subclavian, or left common carotid arteries. *L. G. Blair*

261. **An Evaluation of Portal Venography Performed by Intrasplenic Injection of Contrast Material (Splenography)**
F. J. BONTE, A. S. WEISBERGER, and C. PIAVELLO. *Radiology* [*Radiology*] **66**, 17–23, Jan., 1956. 6 figs., 15 refs.

Percutaneous splenography is a comparatively new radiological technique which is still in the experimental stage. At the Western Reserve University School of Medicine and University Hospitals of Cleveland, Ohio, splenography was performed in 18 cases, in one of which it resulted in splenic rupture requiring emergency splenectomy. The authors consider that the cause of this complication was fixation of the needle by perforation of the rib periosteum so that the needle did not move with respiration. They state that to avoid rupture of the spleen the needle must be inserted through the mid-point of the 9th or 10th interspace. A free flow of aspirate must be obtained before contrast material is injected to ensure that the needle is correctly inserted.

The importance of careful selection of patients for this examination is emphasized; if splenectomy is contra-indicated for any reason, then splenography should not be considered. In 10 of the authors' cases the results of splenography were unsatisfactory.

D. E. Fletcher

262. **New Means of Radiological Investigation of the Biliary Tract Provided by "Biligrafin".** (Durch Biligrafin eröffnete neue Wege für die Röntgenuntersuchung des Gallensystems)
S. LAJOS. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **83**, 776–784, Dec., 1955. 5 figs., 33 refs.

The author describes a technique developed at the Medical Clinic of the University of Szeged, Hungary, for increasing the density of the gall-bladder shadow and obtaining more accurate visualization of the common bile duct and the hepatic ducts in cholecystography and cholangiography with "biligrafin". The injection of morphine subcutaneously at the time of injection of biligrafin has been shown to improve visualization by increasing the tone of the sphincter of Oddi and also by

producing a better flow of bile and dilating the gall-bladder. The author claims that still better results can be achieved by giving two doses, each of 20 ml., of biligrafin, the second dose being given, together with 10 mg. of morphine, 2 hours after the first. He states that there is evidence that with a normally functioning gall-bladder a mechanism exists which maintains a constant pressure in the hepatic and common bile ducts and prevents the adequate filling of the latter with biligrafin. This compensatory mechanism is temporarily exhausted by filling the gall-bladder with the first dose of biligrafin, the second dose then filling the ducts more satisfactorily. In 30 cases which were examined by this method excellent visualization of the bile ducts and gall-bladder was obtained; in 5 of these cases examination was carried out subsequently by a single-dose technique without morphine, comparison showing that the density of the shadow of the gall-bladder and bile ducts was less than that by the recommended method.

The author points out that the use of morphine has a number of disadvantages. Emptying of the gall-bladder after a fatty meal cannot be tested, as morphine acts as a dilator of the gall-bladder. Furthermore, morphine causes the emptying of the gall-bladder to be delayed up to 36 to 48 hours, which might result in reflux of the contrast medium into the pancreatic ducts. Again, the effect of morphine may obscure the presence of "stenosing" or "spontaneous" papillitis of the sphincter of Oddi as a result of cholelithiasis.

M. E. Grossmann

263. **Observations on the Bile Ducts after Cholecystectomy.** (Beobachtungen an den Gallenwegen nach Cholezystektomie)

F. Heuck and F. Leupold. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **83**, 784–792, Dec., 1955. 4 figs., 13 refs.

The findings in 52 cases in which intravenous cholangiography with "biligrafin" was carried out after cholecystectomy are described from the Medical Clinic of the University of Kiel. The patients are divided into four groups: (1) those with biliary calculi; (2) those with pathological changes in the bile ducts, such as dilatations, stenosis, adhesions, or kinks; (3) those with symptoms but without positive *x*-ray findings; and (4) those with fistulous communications with the gastro-intestinal tract.

Among the observations made, the following are of interest. Patients in the first two groups may be completely symptomless. Some time after cholecystectomy the stump of the cystic duct may dilate and take over the reservoir function of the gall-bladder (the differential diagnosis between the appearance in such cases and shadows caused by diverticula, a double gall-bladder, and contrast medium in the duodenal cap is discussed). Cholagogues may cause contraction of both the normal and the dilated common bile duct. The function of the sphincter of Oddi cannot be investigated by radiological means. The authors also stress the well-known fact that fistulae between the biliary and gastro-intestinal tracts cannot be demonstrated by cholecystography or cholangiography.

[The authors' correlation of symptoms with *x*-ray signs is well worth studying in the original.]

M. E. Grossmann

264. **Intravenous Cholangiography in the Post-cholecystectomy Syndrome**

C. Don and H. Campbell. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **7**, 197–206, Jan., 1956. 11 figs., 20 refs.

Intravenous cholangiography with "biligrafin" was carried out at University College Hospital, London, on 23 patients suffering from the post-cholecystectomy syndrome and on a further 39 cholecystectomized patients without symptoms. A stone in the common bile duct was found in 4 of the patients with symptoms, but none in the control group; in a further case a stone in the cystic-duct stump was giving rise to symptoms. Cystic-duct stumps were found in 3 cases and kinking of the duct in one case among the 23 with symptoms, but again none in the controls. Dilatation of the ducts was observed with great frequency in both groups; constricted ducts were found more often in the patients without symptoms. The emptying rate was also extremely variable in the control group.

It is concluded, therefore, that (1) stones in the common bile duct or a cystic-duct stump are of definite significance in causation of the syndrome; (2) persistent cystic-duct stump and distortion of the ducts are of probable significance; and (3) dilatation or constriction of the ducts and biliary stasis are in themselves probably of no significance.

L. G. Blair

265. **Contrast Radiography in the Diagnosis of Volvulus of the Small Intestine.** (Значение контрастного рентгенологического исследования в диагностике заворото тонкой кишки)

V. I. Petrov and I. V. Telegin. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **33**, 70–72, No. 11, Nov., 1955. 3 figs., 4 refs.

Although plain radiographs taken in the antero-posterior position provide no help in the differential diagnosis between strangulation and volvulus of the small intestine, the authors state that lateral views may do so, since, when the patient is turned from one side to the other, the loops of the gas-filled intestine change their position in volvulus, whereas they remain fixed in strangulation. A surer diagnosis may, however, be made by employing a barium enema. By this method there can often be seen a smooth, oval indentation of the caudal edge of the shadow of the transverse colon, just to the right of the midline, which is caused by the upward pressure of the underlying twisted mesentery. The caecum and ascending colon are also often lifted upwards towards the liver by pressure of the distended coils of small intestine, and in volvulus, if the intestine is twisted through more than 180 degrees, the stomach may be displaced to the left; this twist is stated to be nearly always in a clockwise direction.

Similar radiographic appearances were obtained by the authors during experiments in which volvulus was produced in the cadaver.

L. Firman-Edwards

266. **Roentgen Findings in Regional Enteritis**
R. H. MARSHAK and B. S. WOLF. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 74, 1000–1014, Dec., 1955. 12 figs., 19 refs.

In this paper from the Mount Sinai Hospital, New York, the radiological findings in 750 cases of regional enteritis observed for periods of 1 to 12 years are described. The precise time of onset of the disease can rarely be determined, and it is usually well established when the patient first attends for radiological examination. The length of bowel involved at this stage represents the maximum and, apart from recurrent disease following exclusion operations, extension does not occur. Clinically, there is usually a low-grade fever, loss of weight, abdominal colic, diarrhoea, and occasionally incomplete obstruction. Pathologically, the affected bowel is thickened, primarily owing to inflammatory hyperplastic changes in the submucosa. The mucosa ulcerates, particularly on the mesenteric side, the mesentery becoming greatly thickened and oedematous, with enlargement of lymph nodes. Fistulae may form and eventually there is a varying degree of cicatrization.

The earliest changes demonstrable radiologically are blunting, flattening, thickening, and straightening of the valvulae conniventes so that they become arranged symmetrically and parallel. Later, owing to submucosal and mucosal thickening, the folds become thicker, irregular, and partially fused and the lumen of the bowel becomes irregular. When ulceration occurs a more characteristic pattern, with longitudinal streaks of barium in the ulcer craters, appears. With further destruction of the folds a " cobblestone " pattern may result, and this is eventually replaced by an irregular network of interlacing streaks of barium. Residual islands of inflamed and hypertrophic mucosa may produce multiple polypoid filling defects, but malignant change does not occur. The bowel becomes narrowed first by oedema, retaining some mobility, but with the development of fibrosis it becomes a straightened, rigid, narrow tube. " Skip areas " of normal intestine intervening between the diseased loops are a characteristic feature. In the stenotic phase further constriction of the intestinal lumen occurs, producing a rigid, " pipe-stem " appearance, and there may be marked dilatation of the proximal bowel, which is not primarily involved in the disease though secondary inflammatory changes, tension ulcers, and muscular hypertrophy may develop owing to the presence of retained secretions.

The characteristics of the disease vary according to the site of involvement. In the terminal ileum, which was involved in 506 of the authors' 750 cases, the characteristic " string sign " occurs, though in the early stages it may be due to spasm only and may even be replaced by distension. Ulceration is frequently marked at this site and fistulae are common. Deformity of the caecum and ascending colon, which are not themselves involved, may result from thickening of the mesentery and from the formation of fistulae between the ileum and the colon. When the upper ileum is involved (102 cases), ulceration and fistulae are less frequent, while skip areas are common. Involvement of the jejunum (12 cases) or the duodenum (4 cases) is characterized by the presence of single or multiple areas of stenosis with proximal dilatation; ulceration is minimal and fistulae are uncommon.

The combination of regional enteritis with diffuse ulcerative colitis is rarely found, but right-sided colitis occurred in 20 cases. Such cases have to be differentiated from cases of ulcerative colitis with " backwash " involvement of the terminal ileum, which occurs in 8 to 20%, and in which narrowing is less marked, rigidity and fistulae are rare, and there is no proximal dilatation.

[This is a valuable paper.] *G. Ansell*

267. **Ankylosing Spondylitis**
J. H. MIDDLEMISS. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] 7, 155–166, Jan., 1956. 28 figs.

Ankylosing spondylitis is a self-limiting disease, affecting predominantly young males; it may be arrested at any point, or may run its full course, ending with ossification of the tissues involved, that is, primarily connective tissue. The sites mainly involved are the sacro-iliac joints and the joints and ligaments of the spine; other sites, however, are not uncommonly affected especially around the pelvic girdle, for example, the symphysis pubis, the outer borders of the iliac bones, and the ischial tuberosities.

The radiological changes are those of bone destruction followed by repair; thus, there is osteoporosis of the cortex, followed by bone reaction, calcification, and re-ossification; the last-named extends beyond the original bone margin but still remains in the connective-tissue planes. The disease is progressive, usually starting in the sacro-iliac joints, the spine being then involved in an ascending direction, though some areas of the spine may be spared. Involvement of the connective-tissue attachments, especially those of the greater trochanter, the os calcis, and also of the joints of the extremities may occur, usually as a late manifestation. The detailed bone changes in the peripheral joints are indistinguishable from those seen in rheumatoid arthritis, but the over-all pattern is different. (The main differences are set out in parallel columns in the original paper.)

The author points out that the general radiological pattern of ankylosing spondylitis in women differs from that in men; in the latter the so-called " bamboo spine " is the typical appearance, whereas women tend to show the " streaky " type of spine. The common features of the disease in females are thus: (1) marked involvement of the posterior spinal articulations; (2) little or no ligamentous ossification; (3) osteoporosis; and (4) often considerable calcification of the costal cartilages.

It is stressed that the radiological appearances of ankylosing spondylitis can be explained in terms of inflammation, reaction, and repair. *L. G. Blair*

268. **Radiological Aspects of the Bony Lesions of Leprosy.** (Aspects radiologiques des lésions osseuses de la lèpre)
A. NÈGRE and R. FONTAN. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] 36, 141–154, 1955. 33 figs., 12 refs.

History of Medicine

269. **Influence of the Society of Apothecaries upon Medical Education**
Z. COPE. *British Medical Journal* [*Brit. med. J.*] **1**, 1–6, Jan. 7, 1956. 3 figs.

From 1617, when James I granted a charter to the "apothecaries of our city of London" and dissolved their ancient connexion with the Grocers, the Society of Apothecaries had the chief formative influence on the medical profession in England and Wales. In particular, the Society was responsible for the emergence of a new type of medical man—the general practitioner. At that time the College of Physicians was a small body of men who had received a wide general education but little clinical training. The Barber-Surgeons, the other main branch of the profession, knew very little medicine. The physicians were forbidden to carry out any manual operations and the surgeons were not allowed to treat internal complaints. Quite apart from these restrictions, the number of physicians and surgeons was hopelessly inadequate for the needs of the rapidly increasing population. Although there was nothing in the Apothecaries' Charter forbidding them to treat internal complaints, their attempts to do so were long resisted by the physicians. In 1704 the House of Lords decided that an apothecary could, without the advice of a physician, prescribe for a sick patient who sought his advice. The fact that he was not allowed to charge for advice but only for the medicine which he made up is probably responsible for the public's abiding faith in the traditional bottle of medicine. After the separation of the barbers from the surgeons in 1745 many of the latter also did medical work, but their training did not make them experts in pharmacy. Except for a few anatomical demonstrations, the Colleges gave no regular teaching, and the pressing need for courses of instruction led to the rise of private schools. The Apothecaries had from the beginning tried to maintain a good educational standard, and from 1633 onwards physicians were invited to be present at the examination of those made freemen. The greatest contribution of the Apothecaries in the educational sphere was the seven-year apprenticeship system, which was more strictly insisted upon than that of the surgeons.

At the beginning of the 19th century there were still no generally accepted standards of medical training, no curriculum, and no real tests of efficiency. The medical corporations were apparently quite unconcerned about this, and the impetus to reform came from the rank and file of the profession. At a meeting of the Lincolnshire Medical Benevolent Society in 1804 Dr. Edward Harrison raised the question of medical reform, and later put forward a scheme which was embodied in a Bill providing for the establishment of a medical register. Because of the obstructive tactics of the medical corporations this scheme failed, and after six years Harrison gave up the struggle. The movement he had started, however, was taken up by the newly-formed Association of Surgeons and Surgeon-Apothecaries under the leadership of Dr. George Man Burrows, and the efforts of this body finally led to the passing of the Apothecaries Act of 1815. This Act gave the Apothecaries power to license a body of practitioners who were entirely independent of the Colleges of Physicians and Surgeons.

During the crucial period between 1815 and the passing of the Medical Act of 1858 the Apothecaries exerted a powerful influence on medical training and practice throughout the country. The apprenticeship system was retained, and to it were added obligatory attendance at hospital or dispensary practice and formal lectures. By 1835 the curriculum had been brought into line with the rapidly increasing body of scientific knowledge. The establishment of a definite curriculum and of a carefully conducted examination had a profound effect on the teaching of medicine and was directly responsible for the foundation of new schools in the provinces. The London hospitals were stimulated to put their own houses in order, and many of the great metropolitan medical schools date their continuous existence from this period. The private medical schools, which had performed great service in their day, gradually faded out or were swallowed up by the hospital schools. The enormous improvement in the standard of medical practice and in the status of the practitioner during the nineteenth century was mainly due to the conscientious way in which the Society of Apothecaries had discharged the onerous duties laid upon it by the Act of 1815. *W. J. Bishop*

270. **The History of Anatomy in Medical Education**
B. J. ANSON. *Quarterly Bulletin of Northwestern University Medical School* [*Quart. Bull. Northw. Univ. med. Sch.*] **30**, 80–94, 1956. 4 figs., bibliography.

271. **Thomas Sydenham: The Father of English Medicine**
K. HIRSCHFELD. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 265–276, Feb. 18, 1956. 5 figs., 29 refs.

272. **Dr. Addison and His Work**
P. M. F. BISHOP. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 1032–1038, Dec., 1955. 1 fig., bibliography.

Thomas Addison's claim to be regarded as the founder of endocrinology rests on his monograph of 1855, in which he described the clinical features of adrenocortical deficiency, showing for the first time that a general morbid condition could be due to a defect of a ductless gland. One of the immediate effects of this monograph was to inspire Brown-Séquard to remove the adrenal glands from a number of experimental animals; from the fact that all the animals succumbed he deduced that the glands contained a principle essential to life. But it was forty years before there was any further advance in

knowledge of the adrenal glands, when the presence of a pressor amine in the medulla was demonstrated. Only during the last twenty-five years have adrenal cortical secretions been seriously studied. (A full bibliography includes references to the major discoveries.)

A general physician with a particular interest in diseases of the chest, Addison was also a distinguished dermatologist. He drew attention to the peculiar discoloration of the skin in pernicious anaemia, and in 1849 he gave what is probably the first accurate clinical picture of this disease. The author discusses the question of whether or not Addison can truly be said to be the discoverer of "Addison's anaemia". The great reputation of Addison during his life-time was due to his qualities as a teacher and to his personal influence on his pupils, who were almost his disciples, during forty years' teaching at Guy's Hospital. His monograph *On the Constitutional and Local Effects of Disease of the Supra-renal Capsules* did not appear until near the close of his career. *Kenneth Stone*

273. **The Causes of Infantile Convulsions Prior to 1900**
J. RENDLE-SHORT. *Journal of Pediatrics* [*J. Pediat.*] **47**, 733–739, Dec., 1955. 37 refs.

Infantile convulsions were commoner in the past than they are today. Buchan in 1776 regarded them as the commonest cause of infant deaths. In the writings of Hippocrates they were ascribed to teething, and Sydenham in the 17th century recommended bleeding for convulsions during dentition in the ninth or tenth month. By the end of the 18th century, however, other causes of convulsions were being suggested, including tight swaddling clothes, water on the brain, worms, and the contagion of such diseases as smallpox and measles. North in 1826 first linked rickets with fits and spasmophilia, the last named having been described by Clark in 1815. It does appear that during the 18th century there was a greatly increased incidence of fits simultaneously with a rise in the incidence of rickets and a fall in the calcium content of the diet of the general population. By 1893 Gowers declared that the majority of cases of "teething convulsions" were due to rickets.

Birth injury was the commonest cause of neonatal fits, and the author of the present paper draws attention to the lack of obstetrical skill, the main causative factor, which prevailed until the influence of William Smellie began to be felt. In many cases febrile convulsions occurred at the onset of smallpox or bacterial meningitis, and a quotation from Morgan (1735) on teething fits reads like a description of meningococcal meningitis. The recent report from the United States of the occurrence of fits in children given pyridoxine-free milk and the control of the fits by administration of pyridoxine prompts the suggestion that "pap", the usual staple food at 9 to 10 months, may well have lacked this vitamin. Another, though less frequent, cause of convulsions was lead poisoning, resulting in encephalopathy; the author points out that this could well have arisen from the use of lead pastes and lead nipple shields by nursing mothers and also of poor pewter with a high lead content for cooking and storage vessels. Finally, worm infestation, especially cysticercosis, doubtless encouraged by the poor hygiene and sanitation, might also have been a cause of fits. *A. White Franklin*

274. **Historical Notes on Cardiac Massage.** (Historisches zur Herzmassage]
E. LESKY. *Wiener klinische Wochenschrift* [*Wien. klin. Wschr.*] **68**, 123–125, Feb. 17, 1956. 11 refs.

275. **A Contribution to the Study of the History of Leprosy.** (Contribución al estudio de la historia de la lepra)
T. RODRÍGUEZ MORENO and F. MONTES BRAVO. *Actas dermo-sifiliográficas* [*Act. dermo-sifiliogr.* (*Madr.*)] **47**, 83–100, Nov., 1955. 28 refs.

Leprosy is one of the most ancient of diseases and its interesting history has been the subject of much discussion. This paper [which adds little to existing knowledge] deals with the history of leprosy in Southern Spain from the earliest times to the present day. Various hospitals, and in particular the Royal Hospital of San Lazaro in Seville, concerned themselves with the care of lepers as far back as the 13th century, when the Kings of Spain themselves engaged in philanthropic schemes on their behalf.

[Unfortunately, the account of this important phase of medical history is not attractively presented by the authors, and makes rather dull reading. Probably the most useful part of the article is the bibliography.]
Douglas Guthrie

276. **The History of the Ovary.** (Storia delle ovaie)
M. SPALLONE. *Humana Studia* [*Hum. Stud.* (*Roma*)] **7**, 164–182, 1955. Bibliography.

Although the ovary was unknown to Hippocrates, it was recognized by Herophilus (*c.* 300 B.C.) who thought it was identical with the testicle—hence Galen's concept of "testes muliebres" producing "female sperm". This view persisted for centuries until Matteo de' Gradi (d. 1480) first named the organs "ovaries", and compared them to those of birds, a view which was adopted by Steno, Graaf, and others. With the advance of human dissection the idea of "female sperm" was finally disposed of by Fallopius, whose pupil Fabricius di Acquapendente also came to the conclusion that most live-born animals developed from the ovum. In 1650 Langly suggested that the ovary of animals should not be regarded as *testis* but as *ovarium*. Steno's researches in comparative anatomy revealed in the female genital gland the ovarian follicles (already noticed by Vesalius); he suspected these to be ova and hence emphatically rejected the term *testis* in favour of *ovary*. His view was supported by Graaf, the weight of whose opinion enabled it to make headway.

Surgery of the ovary was first performed in 1701, and was practised fairly extensively in the late 1850's by Spencer Wells, Lawson Tait, and Battey. The endocrine function of the organ had already been noticed, and in the second half of the 19th century experiments were made with ovarian grafts and extracts. The influence of the follicular hormone on the formation of fibro-

myoma of the uterus was first noted and described by Tridondani in 1889.

The modern history of the ovary began in 1917 with the discovery by Papanicolaou and Stockard of the oestrus phenomenon, which enabled the effect of ovarian hormones (or their absence) to be studied: female sexual biochemistry was thereby placed on a scientific basis. Since 1898 the corpus luteum had been thought to secrete a hormone (a word first used shortly afterwards by Sterling to denote an exciting agent) and its function and effects were determined by subsequent research. In 1922 Allen and Doisy evolved their test for the identification of oestrogen which has formed a basis for all the later investigations in this field—here briefly outlined.

In conclusion, the author emphasizes that although the results of extirpation of the male sex gland were known in antiquity, the knowledge of the reproductive and endocrine functions of the ovary was delayed for nearly 2,000 years by Galen's erroneous teaching, and most of the discoveries concerning it have been made since 1917. Moreover the history of medicine shows that this is not an isolated example of the long struggle necessary to remove mistaken concepts. *G. R. Pendrill*

277. **De Haemorrhois. A Study in Surgical History** A. G. PARKS. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 135–156, 1955. 6 figs., bibliography.

Because the anal canal is singularly resistant to infection by trauma, anal diseases have been treated surgically from very early times. In this paper the history of the treatment of haemorrhoids is told in quotations from medical writers through the ages.

Conditions resembling piles are described in Egyptian papyri, but no mention is made of operative treatment, which was first advocated by the Greeks. Hippocrates, in *The Regimen*, favours ligation, but believing in the beneficial effects of blood-letting, he advises that one haemorrhoid should always be left, a view which persisted through the centuries. The Hippocratic treatise, *On Haemorrhoids*, is thus considered to be of doubtful origin, since it advocates cauterization of all haemorrhoids. Of the Roman authors, Celsus mentions ligation and the ligation–excision techniques, refers to the retention of urine in the postoperative period, and warns against the excessive removal of anal tissue. From Celsus emanated the practical suggestion that the lowest haemorrhoid should be the first to be removed. Galen's treatment consisted mostly of polypharmacy, but he was prepared to operate if necessary. The best ancient account of haemorrhoids and the surgery of this condition is that given by Aetius of Amida (A.D. 527–565), who advocated total removal. His method of stopping bleeding from haemorrhoids, by twisting, anticipated that of Astley Cooper.

Descriptions of the traditional methods of cauterization, ligation, and excision are found in writings of Indian and Arabian authors and in the works of the mediaeval barber-surgeons, but no fundamental advance was made until the 18th century. In 1749 Morgagni provided the first scientific account of the cause of haemorrhoids, which he attributed to the great length of the superior haemorrhoidal vein. In 1774 Jean Louis Petit described the technique of submucosal haemorrhoidectomy, but the universal acceptance of this procedure had to await the advent of general anaesthesia.

During the 19th century various methods of treatment were favoured, including application of nitric acid, injection with phenol solutions, and again cauterization. Early in the century, however, Frederick Salmon of St. Mark's Hospital used an improved ligation procedure, and his technique as later modified by Milligan and others in 1937 is now the standard operation. The Whitehouse operation, introduced in 1882, which entails suture of the rectal mucosa to the anal skin, has unpleasant sequelae and provoked considerable controversy; it is no longer performed in Britain, but has retained a measure of popularity in the U.S.A.

F. M. Sutherland

278. **A Chapter of Egyptian Paediatrics—Breast Feeding.** (Un chapitre de pédiatrie égyptienne: l'allaitement) F. JONCKHEERE. *Æsculape* [*Æsculape*] **36**, 203–223, Oct., 1955. 13 figs., bibliography.

In ancient Egypt breast-feeding by the mother was by far the most usual, if not the only, method of infant feeding among the lower orders of society and representations of this act are less rare than has been generally supposed. From an analysis of the illustrations on Egyptian potsherds and carvings the author describes the five positions usually adopted by the mother when suckling an infant. Few representations of feeding by a royal mother are found, but numerous such representations of goddesses exist, especially of Isis, the Mother-Goddess. Many portrayals are found also of feeding by wet-nurses, who in Court circles were often ladies of noble birth and whose daughters were even allowed the title of " sister of the Pharaoh ". Nevertheless the title may have been more honorific than exact, the lady chosen putting the royal infant to her breast for a few moments at her inauguration, while the actual feeding was done thereafter by a good wet-nurse. Such symbolic portrayals occur in many scenes of the after-life, where a goddess offers her breast to the dead Pharaoh and thus formally adopts him. Oblations of milk from the breast also occur elsewhere in Egyptian religion.

The period of lactation lasted for three years, and naturally many examples are found of the use of " galactagogues " to prevent a premature drying up of the flow during this time, and of prescriptions to cure " a breast which is ill " (most likely mammary abscess or mastitis). If the secretion failed altogether, recourse was had to the milk of animals such as the cow, goat, sheep, or ass. Representations of children drinking straight from the dug of such animals exist, but the author considers that these are most probably of symbolic (religious) significance, and advances the suggestion that certain small flasks made of horn which have been found in excavations were in fact used as feeding bottles.

In conclusion, he quotes certain instances in which the breast-milk was utilized as a vehicle for the administration of drugs to infants. In some cases the substance

was administered in the milk, or was anointed on the breasts and thus transmitted to the child. But the most interesting observation was that in some cases the medicine was taken by the mother, suggesting that the Egyptians may have been acquainted with the excretion of drugs in milk. Finally reference is made to the frequent appearance of " woman's milk " in Egyptian medical prescriptions. *Geoffrey R. Pendrill*

279. **Social Medicine in the Time of the Pharaohs.** (La médecine sociale au temps des Pharaons)
—. HERPIN. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **140**, 46–47, Jan. 24, 1956.

280. **The Treatise on Plastic Surgery of Gaspard Tagliacozzi, a Surgeon of Bologna in the 16th Century.** (Le traité de chirurgie plastique de Gaspard Tagliacozzi, chirurgien de Bologne au XVI[e] siècle)
P. DUMAITRE. *Æsculape* [*Æsculape*] **36**, 343–355, Dec., 1955. 4 figs.

Tagliacozzi was born at Bologna in 1549, the son of a well-to-do silk merchant, and at the age of 19 entered the Bologna School of Medicine—then the most famous in all Europe—where so many great men had studied or taught. It is almost certain that there he must have heard of rhinoplasty from Aranzio, the professor of surgery. Plastic surgery was probably first practised in the East, where mutilation was often imposed as a punishment. Among western writers, Celsus describes plastic operations on the face, which are mentioned also by Galen and Paulus de Aegineta. Early in the 15th century the Branca family of Sicily and later the Vianeos of Calabria had acquired a reputation for reconstructive surgery of the face, using the skin of the arm, for it was a time when many disputes were settled by the sword, and facial injuries were common. Artificial noses of gold and silver were used to replace the deficiencies thus acquired, as is testified by Paré. Many of the great surgeons of the time thought that fibres from the biceps were used for grafts, but this was expressly refuted by Tagliacozzi in a letter to Mercurialis in 1586, wherein he emphasized that it was the skin of the arm which was used.

Tagliacozzi was now professor of anatomy and surgery and had begun to write an exposition of his methods, a work which was to take him eleven years. During this time he attended the nephew of Ferdinand I, Grand Duke of Tuscany, and also the Duke of Mantua. His book was sumptuously published by Gaspard Bondoni of Bologna in 1597 under the title of *De curtorum chirurgia per insitionem libri duo*. Its 22 engravings (four of which are reproduced in the present paper) trace the progress of a patient through a series of plastic operations on the nose, lips, and ears, showing the instruments used and also a form of strait-jacket for holding the patient's arm immovable while a pedunculated flap from the forearm was transplanted to the nose. Tagliacozzi's book was immensely successful; a pirated edition was published in Venice the same year and another in Frankfurt in 1598. In the following year Tagliacozzi died, and his art was gradually forgotten, partly perhaps owing to the poor results obtained by less skilled practitioners, and partly it may be to rumours (such as the one cited by van Helmont) that heterografts would decay on the death of the donor. Tagliacozzi himself was regarded by some as a sorcerer for daring to alter a part of the human body, and his corpse was disinterred from the convent where it had been buried. Later, satirical references to noses derived from the buttocks were made by Samuel Butler in his *Hudibras* and by Voltaire. Not until 1831 was Tagliacozzi's great work republished, when it was re-edited by Trochsel of Berlin.
Geoffrey R. Pendrill

281. **Nelson's Wounds**
L. P. LE QUESNE. *Middlesex Hospital Journal* [*Middx Hosp. J.*] **55**, 182–187, Dec., 1955. 1 fig., 5 refs.

During his 35 years in the Royal Navy Nelson was wounded four times, and on each occasion he showed an indomitable spirit and sense of duty which made him appear insensible to pain. In July, 1794, at the siege of Calvi in Corsica, he was off duty for only 24 hours after being struck in the face and right eye by gravel thrown up by a bullet. This was the injury which blinded the right eye, probably as a result of severe corneal damage. At the Battle of the Nile, in August, 1798, Nelson received a scalp wound which temporarily blinded him completely, as the damaged flap fell across his remaining eye; yet he was on deck on the evening of the same day.

On July 25, 1797, while in command of a landing party at Santa Cruz, Nelson was struck by a musket ball a little above the right elbow. On the long boat trip back to the flagship *Theseus*, Nelson delayed to pick up survivors from the cutter *Fox*, and refused to board the *Seahorse* for fear of alarming the captain's newly-married wife, who was on board. With his sound arm he helped himself aboard the *Theseus* and told the surgeon to prepare the instruments for amputation. He took no alcohol before or during the ordeal, but was given opium afterwards. It is not certain whether the surgeon was Thomas Eshelby of the *Theseus* or a French Royalist refugee named Ronicet. As one of the ligatures enclosed the median nerve, Nelson suffered considerable pain from the stump, but in December, 1797, the ligature came away spontaneously, the wound healed, and, in March, 1798, he was aboard the *Vanguard* at sea.

The fatal wounding at Trafalgar in 1805 is described at length. Although Nelson realized that the wound was mortal, he retained personal command of the action. He described symptoms of spinal pain and internal haemorrhage in the chest, which were subsequently confirmed by the findings at necropsy, carried out by William Beatty, surgeon of the *Victory*. The cause of death was haemorrhage into the left pleural cavity, although, in any case, the spinal injury would have proved fatal in those days. The body was preserved in brandy and spirits of wine and taken back to England, where it was placed in a coffin made from the mast of the *Orient*, the French flagship at the Nile. After lying in state at Greenwich, it was carried in procession, on January 9, 1806, to London, where it now lies in St. Paul's Cathedral.
F. M. Sutherland